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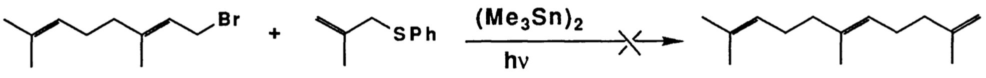
Selective 1,5-Diene Synthesis. A Radical Approach

Akira YANAGISAWA, Yoshiyuki NORITAKE, and Hisashi YAMAMOTO*
Department of Applied Chemistry, Faculty of Engineering,
Nagoya University, Chikusa, Nagoya 464

A new synthetic route to 1,5-dienes is described. Irradiation of a mixture of allyl bromides and allyl sulfides in the presence of hexamethylditin gives the cross-coupled products selectively.

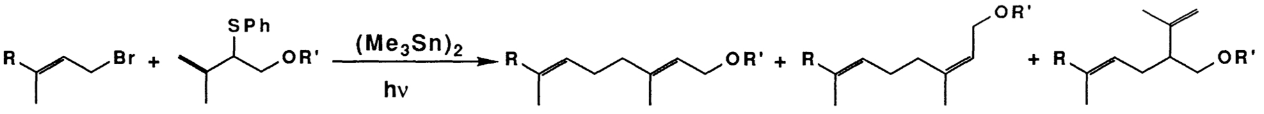
Construction of 1,5-dienes by means of allyl-allyl cross-coupling is an important process from bio-organic and synthetic point of view, and there has been a wide variety of researches on it, but mostly by cationic or anionic approaches.1) Here we wish to report a selective cross-coupling reaction of allyl radicals.

Several recent reports indicated that allyl stannanes2) and sulfides3) reacted with free radical derived from alkyl halides upon heating or irradiation. Unfortunately, however, irradiation of a mixture of geranyl bromide **1** and methallyl sulfide **2** in the presence of hexamethylditin following the conditions reported by Keck3c) afforded only the homo-coupling product of **1** and not the cross-coupling type product 3.



1 **2** **3**

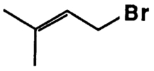
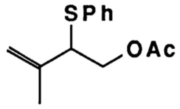
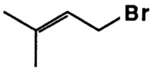
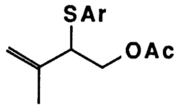
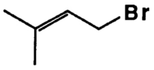
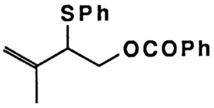
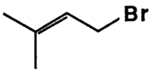
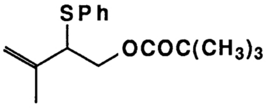
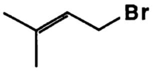
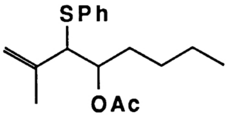
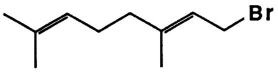
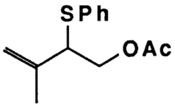
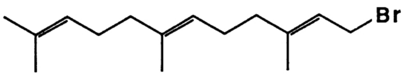
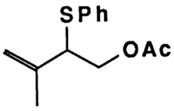
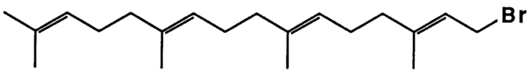
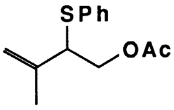
We were surprised to find that cross-coupling reaction does occur between allylic bromides and allyl sulfides of type 5. Thus, photolysis of a mixture of 1-bromo-3-methyl-2-butene (**4**, R=Me, 3 equiv.), 2-(phenylthio)-3-methyl-3-buten-1-ol (**5**, R'=H, 1 equiv.),4,6) and hexamethylditin (2 equiv.) in benzene at 25 °C for 5 h under irradiation (300-W high pressure Hg lamp) gave geraniol (**6**, R=Me, R'=H), nerol (**7**, R=Me, R'=H), and the regioisomer **8** (R=Me, R'=H) in 34% combined yield (ratio, 1.3:1:1.1).7) Further, the acetylated substrate 55,6) (R'=Ac) was even more effective for obtaining the coupling products (57% yield).7)



4 **5** **6** **7** **8**

R=Me; R'=H 34% (1.3:1:1.1)
R=Me; R'=Ac 57% (1.3:1:1.1)

Table 1. Regioselective Allyl-allyl Radical Coupling Reactions[a)]

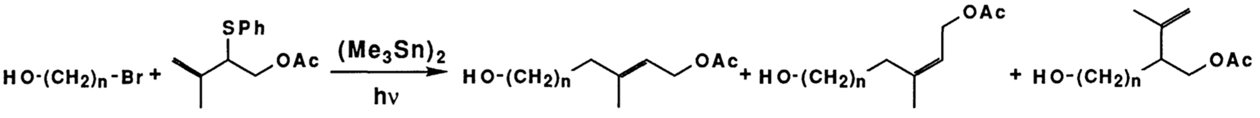
Entry	Allyl bromide	Allyl sulfide	Coupling products[7)] Yield/%[b)] (6:7:8)[c)]
1			57[d)](1.3:1:1.1)
			
2		Ar=2,4,6-(i-Pr)$_3C_6H_2$	16 (1.8:1:1.5)
3		Ar=α-Naphthyl	27 (1.9:1:1)
4		Ar=2,4,5-$Cl_3C_6H_2$	35 (1.3:1:1)
5			59 (1.2:1:1.2)
6			48 (1.2:1:1.5)
7			41 (2.1:1:1.5)[e)]
8			54 (1:1:1.1)
9			59 (1.2:1:1.2)
10			47 (1.5:1:1.2)

a) Unless otherwise specified, coupling reaction was carried out at 25 °C by irradiation (300-W high pressure Hg lamp) of a benzene solution of allyl bromide, allyl sulfide, and hexamethylditin (3:1:2) for 5 h. b) Isolated yield. c) Determined by GC analysis. d) The coupling yield was 62% by irradiation with 1 kW high pressure Hg lamp. e) A mixture of E/Z/γ adduct.

Various types of allyl bromides and allyl sulfides were then subjected to the reaction and the results were summarized in Table 1 which show the following features. (1) The ratio of the coupling products appeared to be dependent of the bulkiness of aryl substituent in allyl sulfide (entries 1 vs. 2 and 3). No significant electronic effect of substituent on the aromatic ring of sulfide was observed in the selectivity (entry 4). (2) The product yield decreased by the choice of the bulky ester moiety in **5** or by the use of allyl sulfide possessing a secondary ester function8) (entries 6 and 7). (3) A various size of allyl bromides9) can be utilized (entries 8—10). No isomerization of the double bond at allylic bromides was observed through the reaction.

The following procedure for the coupling reaction between 1-bromo-3-methyl-2-butene (**4**, R=Me) and 1-acetoxy-2-(phenylthio)-3-methyl-3-butene (**5**, R'=Ac) is illustrative. A solution of 1-bromo-3-methyl-2-butene (**4**, R=Me, 447 mg, 3 mmol), 1-acetoxy-2-(phenylthio)-3-methyl-3-butene (**5**, R'=Ac, 262 mg, 1 mmol), and hexamethylditin (655 mg, 2 mmol) in 5 mL of benzene was placed into a quarts test tube sealed with a rubber septa and degassed with argon for 5 min. The tube was irradiated with a 300-W high pressure Hg lamp at 25 °C for 5 h, at which time no starting material remained by TLC analysis. The crude reaction mixture was treated overnight with excess KF in acetonitrile,10) filtered through an alumina pad, and then concentrated. The residue was purified by column chromatography on silica gel (ether/hexane, 1:50 to 1:20 as eluant) to give a mixture (112 mg) of geranyl acetate (**6**, R=Me, R'=Ac), neryl acetate (**7**, R=Me, R'=Ac), and the corresponding regioisomer **8** (R=Me, R'=Ac) in 57% combined yield as a colorless oil. The ratio of the isomer was determined by capillary GC to be 1.3:1:1.1.

The coupling process is also applicable to a wide range of alkyl halides such as 2-bromoethanol (**9**) and 3-bromopropanol (**10**):3c)



n=2: **9** n=2: **39% (4.9:3.1:1)**
n=3: **10** n=3: **43% (2.6:1.7:1)**

Further study is required before the mechanistic details of these reactions can be understood. However, the broad scope and utility of the method are apparent. It should be noted that the success of the reaction is heavily owed to the activation of C-S bond by the neighboring ester group. In fact, a facile allylic rearrangement of allylic sulfide **5** under irradiation is well known, probably through a radical intermediate.6) Furthermore, such neighboring effect of ester function is observed in the previous mechanistic study of the radical process.11)

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References

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Baker, Chem. Rev., 73, 487 (1973); G. Courtois and L. Miginiac, J. Organomet. Chem., 69, 1 (1974); P. L. Stotter and R. E. Hornish, J. Am. Chem. Soc., 95, 4444 (1973); F. Derguini-Boumechal, R. Lorne, and G. Linstrumelle, Tetrahedron Lett., 1977, 1181; J. Godschalx and J. K. Stille, Tetrahedron Lett., 21, 2599 (1980); Y. Yamamoto, H. Yatagai, and K. Maruyama, J. Chem. Soc., Chem. Commun., 1979, 157; J. Am. Chem. Soc., 103, 1969 (1981); Y. Yamamoto, K. Maruyama, and K. Matsumoto, J. Chem. Soc., Chem. Commun., 1984, 548; Y. Yamamoto, H. Yatagai, Y. Saito, and K. Maruyama, J. Org. Chem., 49, 1096 (1984).

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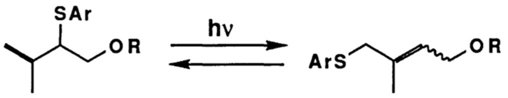
3) a) D. H. R. Barton and D. Crich, Tetrahedron Lett., 25, 2787 (1984); b) D. H. R. Barton and D. Crich, ibid., 26, 757 (1985); c) G. E. Keck and J. H. Byers, J. Org. Chem., 50, 5442 (1985).

4) 2-(Phenylthio)-3-methyl-3-buten-1-ol was prepared from 1-acetoxy-2-(phenylthio)-3-methyl-3-butene5) by hydrolysis with CH_3ONa/CH_3OH.

5) Y. Masaki, K. Hashimoto, and K. Kaji, Tetrahedron Lett., 1978, 4539.

6) Allyl sulfide **5** undergoes very facile allylic rearrangement under irradiation or heating,



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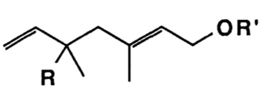
7) Containing small amounts (7—15%) of the corresponding regioisomers as shown below:



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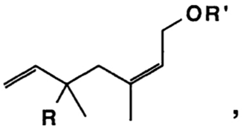

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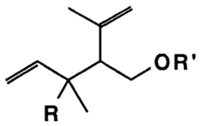

8) Allyl sulfide possessing a secondary ester function was prepared by the reaction between lithiated methallyl sulfide and pentanal in the presence of $Ti(O\text{-}i\text{-}Pr)_4$ followed by acetylation with acetic anhydride/pyridine.

9) Geranyl bromide, (E, E)-farnesyl bromide, and geranylgeranyl bromide were easily obtained by bromination of corresponding alcohols with PBr_3 in ether.

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