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THE STEREOSPECIFIC PREPARATION OF TRISUBSTITUTED OLEFINS

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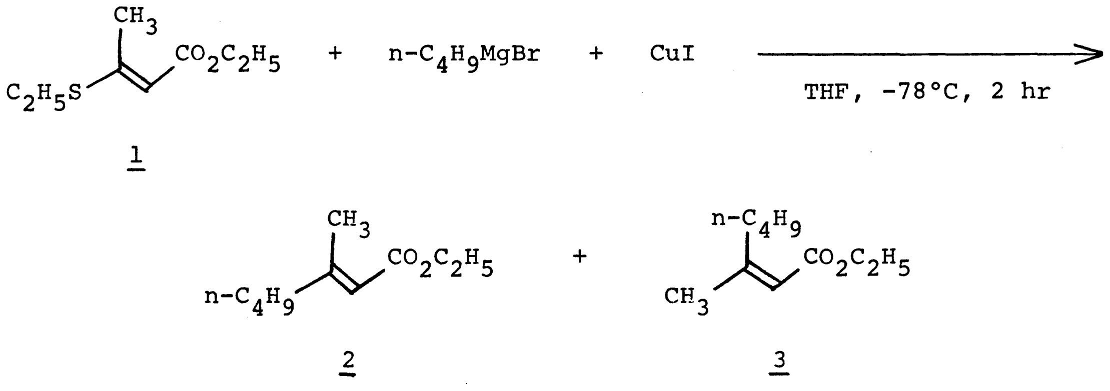
Ethyl (E)-3-methyl-2-heptenoate, 6, or ethyl (Z)-3-methyl-2-heptenoate, 8, was prepared in high yield with the perfect retention of configuration by the reaction of ethyl (E)-3-phenylthio-2-butenoate, 5, or (Z)-3-phenylthio-2-butenoate, 7, with n-butylmagnesium bromide and cuprous iodide, respectively.

The stereospecific or stereoselective synthesis of trisubstituted olefins has been widely investigated with interest to the juvenile hormones and olefinic precursors for cyclization to condensed terpenes and steroids. Recently, Casey et al. reported a new synthesis of substituted α,β-unsaturated ester starting from enol acetate of β-keto ester.1) Here we report a new approach to the stereospecific preparation of trisubstituted olefins by the reactions of ethyl 3-ethylthio- or 3-phenylthio-2-butenoate, 1, 5, 7, with Grignard reagents in the presence of cuprous iodide.2)

It was found that when ethyl (E)-3-ethylthio-2-butenoate, 1,3) was treated



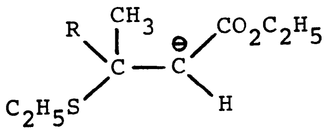
with the mixture of 5 molar amounts of n-butylmagnesium bromide and 2 molar amounts of cuprous iodide in tetrahydrofuran at -78°C for 2 hr, ethyl 3-methyl-2-heptenoate, 2 and 3, was obtained in 94% yield, and the ratio of ethyl (E)-, 2, to (Z)-3-methyl-2-heptenoate, 3, was 90 : 10 from vpc analysis. The stereochemistry of (E) and (Z) isomers was characterized by the difference of the chemical shift of methyl proton at side chain; the methyl proton of the (E) isomer reveals at δ 2.12 and that of the (Z) isomer reveals at δ 1.86, respectively.

In a similar manner, the vinyl sulfide 1 was treated with several Grignard reagents, and the results are shown in the following Table.

Table Reaction of 1 with RMgBr in the presence of CuI

R	Yield (%)	(E) : (Z)
C_2H_5	96	90 : 10
n-C_4H_9	94	90 : 10
n-C_6H_{13}	96	90 : 10

The ratios of (E) to (Z) obtained in these experiments show that the reaction proceeds through a stereospecific replacement of ethylthio group by alkyl group with retention of configuration. The partial loss of stereochemistry would be probably due to the relatively stable carbanion, 4, from which both (E) and (Z) isomers are produced by the removal of thiolate anion. If such is the case, when phenylthio analogue of vinyl sulfide 1 is employed as a substrate, the increase of the stereospecificity would be achieved, since it is generally known that phenylthio group is more facile to be eliminated as an anion than ethylthio group.



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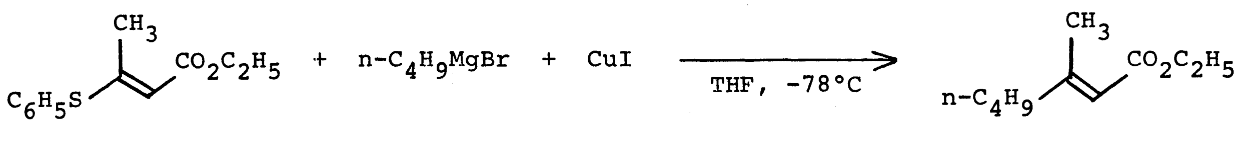
In fact, when ethyl (E)-3-phenylthio-2-butenoate,[4] 5, (451.8 mg, 2.0 mmol) was treated with n-butylmagnesium bromide (10.0 mmol) and cuprous iodide (795.8 mg, 4.2 mmol) in 25 ml of tetrahydrofuran at -78°C for 4 hr, ethyl (E)-3-methyl-2-heptenoate, 6, was obtained exclusively in 94% yield, and none of the (Z) isomer



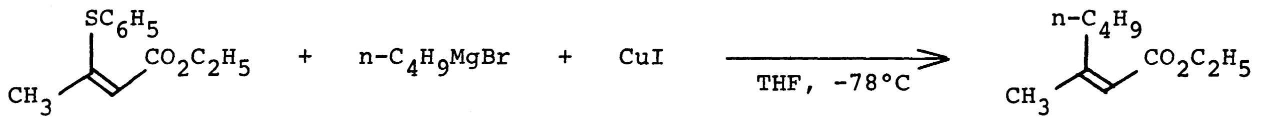
5

6

94% (purity > 99%)

could be detected by vpc analysis.

Further, when ethyl (Z)-3-phenylthio-2-butenoate,[4)] 7, (214.9 mg, 0.97 mmol) was treated with n-butylmagnesium bromide (5.0 mmol) and cuprous iodide (384.7 mg, 2.0 mmol) in tetrahydrofuran at -78°C for 2 hr, ethyl (Z)-3-methyl-2-heptenoate, 8, was isolated in 79% yield with the purity of over 99%, and the starting material 7 was recovered in 14% yield.



7

8

79% (purity > 99%)

The mechanism of this reaction is not yet clarified, however, it is noted that trisubstituted olefins are produced in high yields with the perfect retention of configuration when ethyl 3-phenylthio-2-butenoate is allowed to react with Grignard reagent in the presence of cuprous iodide.[5)]

Further works including the mechanistic study are now in progress and will be reported at a later time.

REFERENCES

1) C.P.Casey, D.F.Marten, and R.A.boggs, Tetrahedron Lett., 1973, 2071.

2) No reaction occurred when the above reaction was carried out in the absence of cuprous iodide.

3) Vinyl sulfide 1, bp 115-120°C/16 mmHg, was prepared by the pyrolysis of ethyl 3,3-bis(ethylthio)-butyrate in the presence of catalytic amount of zinc chloride at 110°C.

4) The method for the preparation of ethyl 3-phenylthio-2-butenoate, 5 or 7, is similar to the case of the vinyl sulfide 1. Pyrolysis of diphenyl thioacetal afforded both ethyl (E)-, 5, and (Z)-3-phenylthio-2-butenoate, 7, (the ratio of 5 to 7 was about 9 : 1), and these isomers were separated by Silica Gel column chromatography. The stereochemistry of (E) and (Z) isomers was determined by nmr spectra: (E) isomer; olefinic proton δ 5.20, methyl proton δ 2.40, (Z) isomer; olefinic proton δ 5.78, methyl proton δ 1.77.

5) No reaction occurred when the vinyl sulfide 5 was treated with lithium di-n-butyl cuprate, n-butylcopper or n-butylcopper in the presence of cuprous iodide in tetrahydrofuran at -78°C.

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