Tetrahedron Letters No. 4, pp 239 - 242, 1976. Pergamon Press. Printed in Great Britain.

# A FACILE ROUTE TO E-4-BROMO-3-METHYL-2-BUTEN-1-OL: APPLICATION TO THE STEREOSELECTIVE SYNTHESIS OF TRISUBSTITUTED OLEFINS

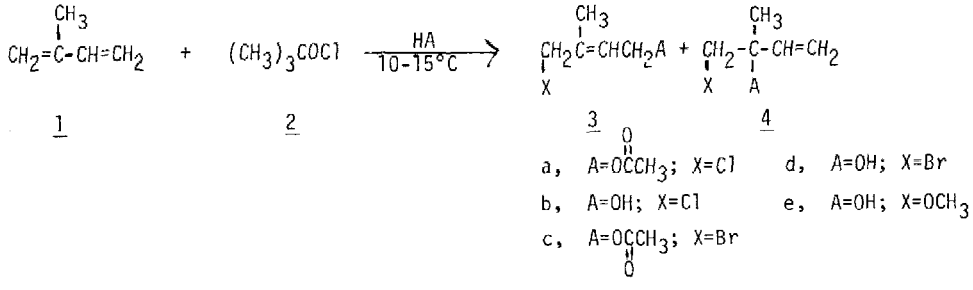
James H. Babler* and William J. Buttner

Department of Chemistry, Loyola University of Chicago

Chicago, Illinois 60626 USA

**(Received in USA 29 September 1975; received in UK for publication 16 December 1975)**

In 1950 W. Uroshnik and R. A. Mallory carried out a study[1] of the addition products obtained upon treatment of isoprene (1) with tert-butyl hypochlorite (2) in several different protic solvents. Using acetic acid as the solvent, these authors reported



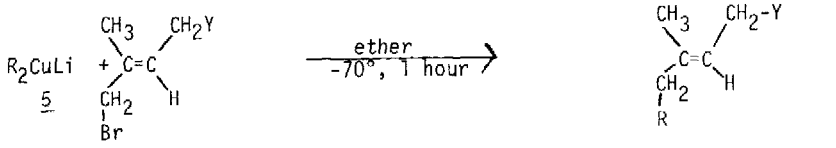
1 2 3 4

a, A=OCCH$_3$; X=Cl d, A=OH; X=Br

b, A=OH; X=Cl e, A=OH; X=OCH$_3$

c, A=OCCH$_3$; X=Br

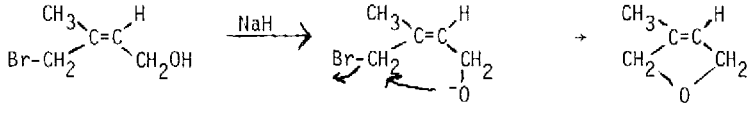
obtaining a 32% yield of the 1,4-adduct (3a) accompanied by 20% of the corresponding 1,2-addition product (4a). When the same reaction was run in water, only a 3% yield of the 1,4-adduct (3b) could be isolated. In view of the synthetic utility of 1° allylic alcohols of general structure 7a and their derivatives and the known[2] propensity of organocopper(I) complexes (5) to couple with allylic halides, we decided to investigate the above reaction further and examine the utility of the 1,4-adduct 3d in the synthesis of trisubstituted olefins,[3] not to mention its potential as a reagent for prenol homologation.[4]



5 6 a, Y=OH b, Y=OCCH$_3$ 7 a, Y=OH b, Y=R

Consistent with the observations[1] of Oroshnik and Mallory, addition of N-bromosuccinimide (NBS) to isoprene using 1:1 water-tetrahydrofuran as the solvent at 25°C afforded bromo alcohol 3d in only 15% yield after fractional distillation. However, addition of NBS (0.52 mole) to a solution of isoprene (0.7 mole) in glacial acetic acid (300 ml) at 25°C afforded, after fractional distillation,[5] a 55% yield of 4-bromo-3-methyl-2-buten-1-ol acetate (3c) as a 70:30 mixture of E:Z stereoisomers,[6] bp 57-65° (0.20 mm).

In order to obtain the pure E stereoisomer (6a), necessary for the stereoselective synthesis of olefins of general structure 7, the acetate mixture (3c) was hydrolyzed using potassium carbonate (1 equiv) in 4:1 $CH_3OH$-$H_2O$ (0.50 M soln) at room temp. for 20 min. Subsequent treatment of the crude saponification product (3d) with sodium hydride (1 equiv) in anhydrous tetrahydrofuran (0.15 M soln) at 15°C for 90 min. afforded after chromatography on silica gel (elution with hexane -10% ether) E-4-bromo-3-methyl-2-buten-1-ol (6a)[7] in 30% overall yield from 1,4-adduct 3c: bp 62-65° (0.10 mm); $\delta_{TMS}(CCl_4)$ 5.76 (broad t, J=6.5 Hz, vinyl H), 4.12 (doublet, J=6.5 Hz, $CH_2OH$), 3.94 (s, $CH_2Br$), 1.81 ppm[8] (s, vinyl $CH_3$). The Z stereoisomeric alcohol (8), under the conditions of the latter reaction, underwent an intramolecular displacement reaction to afford cyclic ether 9.




8 9

Alternatively, the pure E stereoisomeric alcohol (6a) could be obtained directly in approximately the same overall yield by treatment of acetate 3c with potassium carbonate (1.4 equiv) in absolute methanol (0.5 M soln) at 25° for 3.5 hours, followed by chromatography on silica gel in order to remove the undesired hydroxyether 3e. The acetate derivative (6b)[7] of the bromo alcohol 6a was prepared in 90% yield by addition of 1.3 equivalents of acetyl chloride to a solution (0.35 M) of the alcohol in dry benzene containing 1 equivalent of pyridine (reaction time: 30 min at 0°C): bp 60-65° (0.20 mm); $\delta_{TMS}(CCl_4)$ 5.72 (broad t, J=7Hz, vinyl H), 4.57 (doublet, J=7.0 Hz, $CH_2OAc$), 3.95 (s, $CH_2Br$), 2.00 (s, $OCCH_3$), 1.86 ppm (s, vinyl $CH_3$).

Using the conditions previously developed[2] by Corey and Posner for the coupling of

n-alkylcopper reagents with organic halides, freshly prepared E-4-bromo-3-methyl-2-buten-1-ol (6a) was treated with 5 molar equivalents of lithium di-n-butylcopper (5, R=n-$C_4H_9$) in ether (0.05 M soln based on substrate 6a) at -70°C for 1 hour. The reaction was quenched by pouring the mixture into saturated aqueous ammonium chloride. Addition of ammonium hydroxide to dissolve any insoluble copper salts, followed by extraction with ether and short-path distillation, afforded a 96% yield of the previously reported[9] E-3-methyl-2-octen-1-ol (7a, R=n-$C_4H_9$): bp 45-58° (bath temp, 0.05 mm); 98% pure by VPC analysis.[10] The stereospecificity of this coupling reaction was demonstrated by the conversion of a 70:30 mixture of E:Z stereoisomers of bromo alcohol 3d[11] under the same reaction conditions to a 70:30 mixture[12] of E- and Z- 3-methyl-2-octen-1-ol.

Since lithium diorganocuprates are known[2] to couple with allylic acetates, the reaction of lithium di-n-butylcopper with E-4-bromo-3-methyl-2-buten-1-ol acetate (6b) was also examined. According to a literature report,[13] alkylation with allylic rearrangement, rather than direct displacement of the acetate, is often the preferred reaction pathway in similar systems

Using the same conditions for the coupling reaction described above for bromo alcohol 6a, the corresponding bromo acetate (6b) afforded E-6-methyl-6-dodecene (7b, R=n-$C_4H_9$)[7] in 60% yield: bp (bath temp) 90-105°C (2.7 mm); $\delta_{TMS}(CCl_4)$ 5.05 (broad t, J=6.5 Hz, C=C<u>H</u>), 1.57 ppm (broad s, vinyl $CH_3$); >96% pure by VPC analysis.[14] Evidently alkylation via direct displacement is the favored reaction pathway in this system.

In view of their facile preparation from isoprene, alcohol 6a and its acetate derivative (6b) serve as attractive precursors for functionalized olefins of general structure 7a and trisubstituted olefins of structure 7b respectively.

Acknowledgement--The authors are grateful to Research Corporation for financial support of this work.

## REFERENCES


1. W. Oroshnik and R. A. Mallory, J. Am. Chem. Soc., 72, 4608 (1950).

2. G. H. Posner, Org. React., 19, 1 (1972), J. F. Normant, Synthesis, 4, 63 (1972), and G. H. Posner, Org. React., 22, 253 (1975). For a specific example of the coupling of such complexes to organic halides, see: E. J. Corey and G. H. Posner, J. Am. Chem. Soc., 90, 5615 (1968).

3. For two recent reviews, see: D. J. Faulkner, Synthesis, 175 (1971) and J. Reucroft and P. J. Sammes, Quart. Rev., Chem. Soc., 25, 135 (1971).

4. B. S. Pitzele, J. S. Baran, and D. H. Steinman, J. Org. Chem., 40, 269 (1975).

5. The bp of the 1,2-adduct (4c) was 65° at 3.0 mm.

6. Determined by VPC analysis using a 6' x 1/8" SE-30 column at a temp of 133° ($t_R$ of "Z"= 5.1 min; $t_R$ of "E" = 5.7 min). The E isomer was characterized by a singlet at 3.95δ ($CH_2Br$), whereas the corresponding signal for the Z stereoisomer appeared at 4.02δ.

7. Satisfactory elemental analysis (±0.25%) was obtained for this previously unreported compound.

8. The corresponding signal for the Z stereoisomer present in the crude saponification product (3d) appeared at 1.89δ.

9. K. Ogura, et. al., J. Am. Chem. Soc., 92, 6036 (1970).

10. A 6' x 1/8" SE-30 column (T=130°) was used for this analysis (retention time = 4.2 min). An unidentified impurity (retention time = 2.9 min, 2% of the mixture) was shown not to be the Z-alcohol stereoisomer, whose retention time was 3.8 min under the same conditions.

11. Prepared by adding NBS to isoprene in 1:1 $H_2O$-THF.

12. Obtained by NMR as well as VPC analysis. $\delta_{TMS}(CCl_4)$ 1.71 ("Z" vinyl $CH_3$), 1.65 ppm ("E" vinyl $CH_3$).

13. R. J. Anderson, C. A. Henrick, and J. B. Siddall, J. Am. Chem. Soc., 92, 735 (1970).

14. A 6' x 1/8" SE-30 column (T=130°) was used for this analysis. The retention time of the E stereoisomer under these conditions was 8.0 min. Less than 1% of the Z isomer ($t_R$ = 7.1 min) was present in the mixture.