

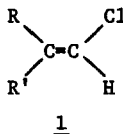
THE STEREOSPECIFIC SYNTHESIS OF VINYL CHLORIDES AND VINYL BROMIDES VIA
ORGANOCOPPER REAGENTS

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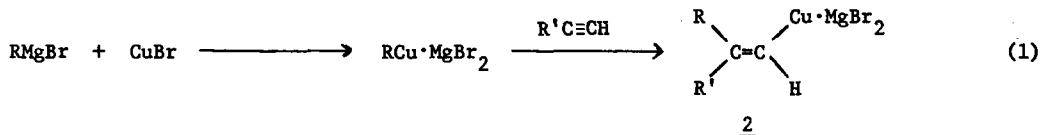
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(Received in USA 30 June 1977; received in UK for publication 18 August 1977)

Recently for a synthetic problem we required stereospecifically defined vinyl chlorides of type 1, for which no simple synthesis appears in the literature. The synthetic method of

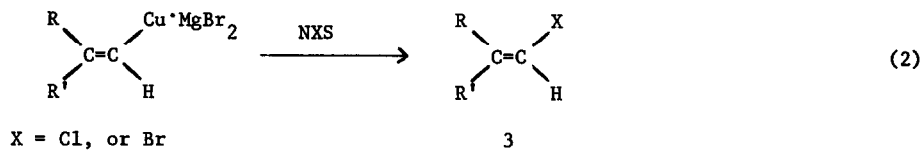


choice would appear to be via Normant's reaction¹ to give the vinylcopper 2 (eq 1).² Subsequent chlorination of 2 would, in principle, lead to 1. While Normant has reported that the



direct iodination of 2 leads to the vinyl iodides with retention of the initial stereochemistry, attempted bromination gives mainly dimers.³ Not surprisingly, dimers are the major products obtained upon attempted chlorination of 2 with Cl₂ in CCl₄. While a circuitous route to vinyl bromides via mercuriation of 2 followed by halogenation of the vinyl mercurial has been reported,³ the analogous route to vinyl chlorides has several disadvantages. Fortunately, we have now found that treatment of 2 with N-chlorosuccinimide at -45°C leads to fair to excellent yields of the corresponding vinyl chlorides. Further investigation showed that the use of N-bromosuccinimide leads to acceptable yields of vinyl bromides also (eq 2). In view of these encouraging results, we undertook a systematic study of the synthetic utility of this sequence.

The results are summarized in Table I.



The syn stereochemistry of this reaction is suggested by analogy with the previous work of Normant and confirmed by the presence of strong bands in the infrared spectrum of 3f and 3j between 700 - 750 cm^{-1} and the absence of bands between 900 - 1000 cm^{-1} . The stereochemical purity of these olefins is a more difficult problem. It is clear from the ^{13}C nmr of 3c and 3d that these compounds are nonidentical. Based on careful analysis of the ^{13}C nmr, we estimate the minimum purity of 3c and 3d to be 96%. Unfortunately, preliminary attempts to analyze the purity of these compounds by capillary gas chromatography have failed to separate the isomers. However gas chromatographic analysis of 3j indicates the initial product to be 99.7% of the Z isomer.⁴

In summary, these developments provide a straightforward route to stereochemically defined vinyl chlorides. Furthermore, this methodology provides an alternative route to stereochemically defined vinyl bromides, without the necessity of utilizing organomercurials as intermediates.

The following procedure is representative.⁵ A dry 1000 ml round bottom flask equipped with a septum inlet and magnetic stirring bar is flushed with nitrogen. To this flask is added 16.14 g (78.8 mmol) of $\text{CuBr} \cdot \text{Me}_2\text{S}$ ^{6,7}, 60 ml of Me_2S and 75 ml of ether under nitrogen. The resultant slurry is cooled to -45°C and 24.75 ml (75 mmol) of a solution of ethyl magnesium bromide added. The solution is stirred for 1 hour at -45°C and 11.1 ml (75 mmol) of 1-octyne added. The flask is warmed to -25°C and stirred for 4 hrs. The solution is then cooled to -78°C and 10.95g (55 mmol) of N-chlorosuccinimide in 250 ml of THF is added. The solution is allowed to warm to -25°C and is vigorously stirred for 1 hour.^{8,9} The resultant solution is hydrolyzed with 50 ml of 10% ammonium hydroxide and 40 ml of saturated ammonium chloride solution. The flask is equipped with an appropriate condenser and the copper(I) byproducts oxidized by bubbling air through the flask for 1-2 hrs. The organic phase is separated, washed with ammonium hydroxide until no blue color appears, dried (K_2CO_3), and the solvent removed by distillation through a 6" Vigreux column. Distillation through a Teflon-coated micro-spinning

Table I. The Reaction of Vinyl Copper Reagents^a 2 with N-Chlorosuccinimide and N-Bromosuccinimide.

| R = | R' = | X = ^b | Vinyl Halide ^c | Yield ^d % |
|--|--|------------------|--|-------------------------|
| C ₂ H ₅ | <u>n</u> -C ₆ H ₁₃ | Cl | <u>E</u> -1-chloro-2-ethyl-1-octene (3a) | 79 (61) |
| C ₂ H ₅ | C ₆ H ₅ ^e | Cl | <u>E</u> -1-chloro-2-phenyl-1-butene (3b) | 63 |
| <u>n</u> -C ₃ H ₇ | C ₂ H ₅ | Cl | <u>Z</u> -1-chloro-2-ethyl-1-pentene (3c) | 98 |
| C ₂ H ₅ | <u>n</u> -C ₃ H ₇ | Cl | <u>E</u> -1-chloro-2-ethyl-1-pentene (3d) | 87 |
| <u>n</u> -C ₃ H ₇ | CH ₃ | Cl | <u>Z</u> -1-chloro-2-methyl-1-pentene (3e) | 57 |
| <u>n</u> -C ₆ H ₁₃ | H ^e | Cl | <u>Z</u> -1-chloro-1-octene (3f) | 50 |
| C ₂ H ₅ | <u>n</u> -C ₆ H ₁₃ | Br | <u>E</u> -1-bromo-2-ethyl-1-octene (3g) | 61 |
| C ₂ H ₅ | C ₆ H ₅ ^e | Br | <u>E</u> -1-bromo-2-phenyl-1-butene (3h) | 54 |
| <u>n</u> -C ₃ H ₇ | CH ₃ | Br | <u>Z</u> -1-bromo-2-methyl-1-pentene (3i) | 72 |
| <u>n</u> -C ₆ H ₁₃ | H ^e | Br | <u>Z</u> -1-bromo-1-octene (3j) | 52 |

^a The vinylcopper reagents were prepared by the method of Normant using CuBr·Me₂S and a 1:1 mixture of ethyl ether and dimethylsulfide as solvent. ^b Commercial N-halosuccinimides were used after careful purification by recrystallization. ^c All compounds exhibited spectral data in accordance with their structure and gave satisfactory elemental composition by high resolution mass spectrometry and/or elemental analysis. ^d Analysis by glpc (isolated yields in parenthesis). ^e When acetylene or phenylacetylene is used, the initial amounts of solvents are cut in half and 5 ml of hexane added prior to the addition of acetylene.

band column gave 7.96 g (61%) of E-1-chloro-2-ethyl-1-octene, Bp 82-84 (35 mm). Calcd. for C₁₀H₁₉Cl: C, 68.76; H, 10.88. Found: C, 69.06; H, 11.08.

Acknowledgement: Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society and to the Research Corporation for support of this work.

REFERENCES

1. J. F. Normant, G. Cahiez, C. Chuit, and J. Villieras, *J. Organomet. Chem.*, 77, 269, 281 (1974).
2. We do not intend to imply any specific structure for the vinylcopper complex.
3. J. F. Normant, C. Chuit, G. Cahiez, and J. Villieras, *Synthesis*, 803 (1974).
4. We have found the vinyl bromides to be configurationally unstable upon standing unless stored in a freezer under nitrogen and in the presence of solid potassium carbonate.
5. Air-sensitive materials were handled by standard methods. See: H. C. Brown, G. W. Kramer, A. B. Levy and M. M. Midland, "Organic Syntheses via Boranes", Wiley-Interscience, New York, N.Y., 1975, Chapter 9.
6. H. O. House, C.-Y. Chu, J. M. Wilkins and M. J. Umen, *J. Org. Chem.*, 40, 1460 (1975).
7. The addition of an organocopper reagent to a terminal acetylene is highly dependent on the purity of the copper salt used. We find $\text{CuBr}\cdot\text{Me}_2\text{S}$ to be the reagent of choice using a 1:1 mixture of dimethylsulfide-diethyl ether as solvent.
8. We used an oversized magnetic stirrer. If stirring is not thorough, the reaction is slow and the yield decreases. The major product in this case is the olefin resulting from protonolysis of 2.
9. Optimum conditions for the bromination differ slightly. We find 2 hours at -45°C followed by hydrolysis to provide the best results.