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A SIMPLE STEREOSELECTIVE SYNTHESIS OF Z-γ-BISABOLENE

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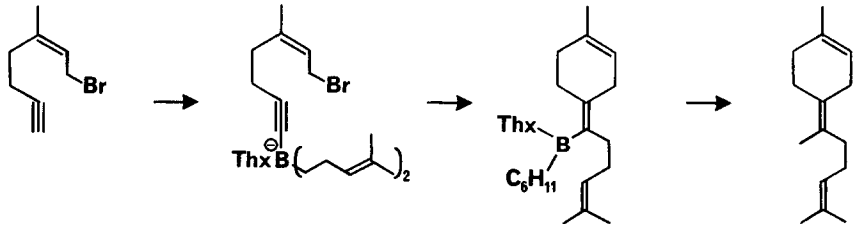
Summary: A simple one-flask synthesis of Z-γ-bisabolene (1) from the acyclic acetylene 2 is described.

The preceding note reports a stereospecific synthesis of E-γ-bisabolene based on the trimethylsilyl trifluoromethanesulfonate-induced rearrangement of an alkynyltrialkylborate complex.[1] This paper describes a stereoselective synthesis of Z-γ-bisabolene (1)[2] which utilizes an alkynyltrialkylborate complex in a different way and takes advantage of an internal carbon electrophile to initiate both cyclization and an alkynylborate⟶alkenylborane rearrangement.[3]

The starting material for the synthesis of 1, 3-methylhept-2-en-6-yn-1-ol,[1] was transformed into the corresponding bromide (2) by reaction with triphenylphosphine-bromine complex (1:1) in methylene chloride at 0° for 15 min. Deprotonation of 2 in tetrahydrofuran (THF) was effected at -78° by phenyllithium and the resulting lithium acetylide was treated at -78° with bis(4-methyl-3-pentenyl)thexylborane[4] to form the corresponding alkynylborate 3 which was allowed to react in the temperature range -78° to 23° over an 8 h period. The resulting cyclic vinylborane 4 was methylated[5] by sequential treatment first with n-butyllithium at -30° for 20 min, then cuprous iodide, triethylphosphite, hexamethylphosphoric triamide, and methyl iodide. After treatment with alkaline hydrogen peroxide to destroy organoboranes and extractive isolation there was obtained 70% of a 79:21 mixture of Z- and E-bisabolenes. The stereoselectivity of the reaction could be increased somewhat by the addition of cuprous triflate to the ethynylborate which provided an 83:17 mixture of Z- and E-bisabolenes in 71% yield. Although it is possible that stereoselectivity could be enhanced under other conditions, this possibility was not exhaustively studied.

The opposite stereochemical courses of the boron to carbon rearrangements induced by trimethylsilyl trifluoromethanesulfonate and carbon electrophiles[1,3,4] is of considerable mechanistic as well as practical interest. As pointed out in the foregoing note,[1] the stereospecific silicon electrophile induced rearrangement can reasonably be interpreted in terms of a bridging siliconium intermediate. The mechanism of the carbon induced rearrangement is less clear.[4] The fact that the reaction is stereoselective (opposite in sense to silicon) but not stereospecific would seem to indicate that a very different mechanism is operating. One interesting possibility involves initial electron transfer (alkynylborate to allylic bromide) followed by attack of the resulting carbon radical on the triple bond.



2 3 4 1

Experimental detail on the conversion of 2 to 1 follows:

A solution of 42 mg (0.227 mmol) of the bromide 2 in 1 ml of THF at -78° was treated with 0.25 mmol of phenyllithium. After 5 min, 74 mg (0.284 mmol) of bis(4-methyl-3-pentenyl)thexylborane was added. The complex 3 was allowed to form for 1.5 min, and a solution of 57 mg (0.227 mmol) of bis(copper(I)trifluoromethanesulfonate)-benzene complex and 106 mg (0.522 mmol) of tributylphosphine in 0.5 ml of THF were added. After stirring for 12 h at -78°, the solution was brought to -30° and butyllithium (0.568 mmol) was added. The orange solution was stirred for 20 min. Addition of 48 mg (0.250 mmol) of cuprous iodide quickly produced a brown-black organocopper specie which was methylated by sequential treatment with 45 mg (0.272 mmol) of triethylphosphite, 0.4 ml of hexamethylphosphoric triamide and 97 mg (0.681 mmol) of methyl iodide. The mixture was allowed to slowly warm to room temperature and oxidized with a solution of sodium hydroxide and 30% hydrogen peroxide. Pentane extraction and analysis by capillary VPC using hexadecane as internal standard afforded Z- and E-γ-bisabolenes (ratio 83:17) in 71% yield along with 7% non-methylated cyclization products.

References and Notes

1. E. J. Corey and W. L. Seibel, Tetrahedron Letters, preceding paper.

2. For natural occurrence and nomenclature see E. Guenther, "The Essential Oils," Vol. 2, p. 81, 1949, D. Van Nostrand Co., Inc. New York.

3. For a review of the chemistry of alkynylborates see E. Negishi in "Comprehensive Organometallic Chemistry," G. Wilkinson, Ed., Vol. 7, p. 337, 1982, Pergamon Press.

4. A. Pelter, T. W. Bentley, C. R. Harrison, C. Subrahmanyam, and R. J. Laub, J. Chem. Soc. Perkin I, 2419 (1976).

5. K. Uchida, K. Utimoto, and H. Nozaki, J. Org. Chem., 41, 2941 (1976).

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