

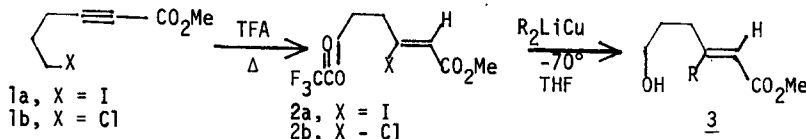
TERPENE SYNTHONS I. INSECT HORMONE BUILDING BLOCKS.

T. A. Bryson

Department of Chemistry, University of South Carolina, Columbia, South Carolina 29208

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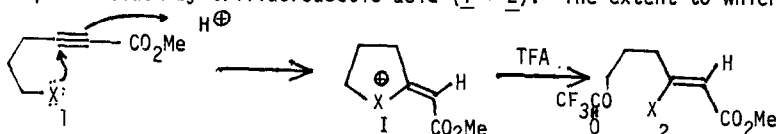
Insect hormones and pheromones have been the object of several recent chemical and biological investigations.¹ Synthetic studies related to several of these compounds are concerned with construction of cis- and trans- trisubstituted olefins. Our finding related to this latter feature of insect chemistry entails stereospecific addition of HX to triple bonds through intramolecular processes. Specifically, trisubstituted olefin precursor, methyl 6-iodo-2-hexynoate (1)² undergoes 1,4-iodide shift in refluxing trifluoroacetic acid (TFA, 50 hr), quantitatively forming methyl 3-iodo-6-trifluoroacetoxy-2-hexenoate (2). Vinyl iodide 2 (1 eq.), on treatment with lithium dialkyl copper reagents (i.e. 1.1 eq of LiCuMe₂) at -70°C in THF, undergoes stereospecific iodide replacement with concomitant trifluoroacetate cleavage forming trans-unsaturated ester 3 [R=Me; CMR(ppm)_{CH₂Cl₂}^{TMS} 37.9 (C₄), 19.2 (C₇); PMR(δ)_{CCl₄}^{TMS} 2.09 (C₇H's coupled to vinyl H)] in 95% yield contaminated with 5% of the cis-ester [R=Me; CMR(ppm)_{CH₂Cl₂}^{TMS} 32.0 (C₄), 25.5 (C₇); PMR(δ)_{CCl₄}^{TMS} 1.86 (C₇H's coupled to vinyl H)].^{3,7} Similar 1,4-halogen shifts



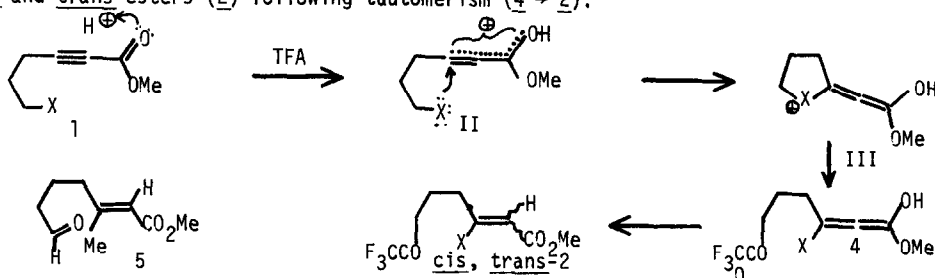
with simple acetylenes have been observed by Peterson and co-workers.⁴ As in this earlier study, the halogen shift occurred exclusively in a trans fashion affording 2, the iodide and carbomethoxy group cis[CMR(ppm)_{CH₂Cl₂}^{TMS} 126.9 (C₂), 119.4 (C₃), 44.8 (C₄), PMR(δ)_{CCl₄}^{TMS} 4.44 (t, J=7cps, 2H, C₆H's), 6.45 (s, broad, 1H, C₂H); ir (film) 1790, 1720 cm⁻¹].⁵ Methyl 6-chloro-2-hexynoate (1b) transfers chloride considerably slower than iodide 1a. After 8 days at 130°C (bomb) in TFA, chloride 1b was converted to vinyl chloride 2 in 30% yield with the recovery of starting material (1b) being 60-65%.

The apparent differences in reaction rates of the haloacetylenic esters cited above and the acetylenes studied by Peterson can be attributed to the deactivating effect of the carbomethoxy group. The exclusive formation of cis-vinyl halide 2 from 1 would seem to be indicative of a

synchronous protonation of the triple bond with halogen shift represented by intermediate I, followed by subsequent attack by trifluoroacetic acid (1 → 2). The extent to which protonation



of the carbomethoxy group (II) enters into this reaction is not readily apparent, since the corresponding halonium ion intermediate III, if formed, would be expected to afford a mixture of cis and trans-esters (2) following tautomerism (4 → 2).



Alcohol 3 has been oxidized to aldehyde 5 (CrO_3 -pyridine/ CH_2Cl_2 , 87% for three steps from 1a) and eventually converted to juvenile hormone using previously described methods offering an interesting alternative to earlier preparations of this same aldehyde.^{7,8} Alternate copper reagents (R=alkyl) have provided olefinic material resembling other key insect hormones.⁹ We are pursuing the compatibility of additional functional groups with acetylene-1,4-halogen transfer.

Acknowledgement: We gratefully acknowledge the Research Corporation and the American Cancer Society (Grant No. IC-83) for support of this work.

1. Insect Juvenile Hormones, Julius J. Menn and Morton Beroza, Academic Press, 1972.
2. Methyl esters 1a and 1b were prepared from 5-halo-pentyne by carboxylation (BuLi/CO_2) and esterification (MeOH/H^+) in 80 to 85% overall yield. All compounds were analyzed by ir, nmr (^1H and ^{13}C), UV, and mass spectra (or analysis).
3. The predicted CMR (proton decoupled, FT) chemical shift for C_4 and C_7 in the cis-compound is 32 ppm and 24 ppm, respectively; and the trans-compound 38-40 ppm and 17-19 ppm respectively, see reference 6 and 7.
4. P. E. Peterson, R. J. Bopp, and M. M. Ago, J. Amer. Chem. Soc., **92**, 2834 (1970).
5. The predicted CMR (proton decoupled, FT) chemical shift for C_2 , C_3 , and C_4 in the cis-compound is 126.1 ppm, 120.0 ppm and 44.8; the trans-compound is 131.6 ppm, 127.7 ppm and 38.0 ppm (respectively). See reference 6 and 7.
6. Carbon-13 NMR Spectroscopy, J. B. Stothers, Academic Press, (1972).
7. The trans geometry of 3 was further supported by oxidation to aldehyde 5, the cis and trans isomers of which have been previously characterized. This earlier preparation of 4 involved a three step procedure from 6-methyl-6-hepten-2-one in 40% yield, reference 8.
8. C. A. Henrick, E. Schaub, and J. B. Siddall, J. Amer. Chem. Soc., **94**, 5374 (1972).
9. S. Bowlus and J. Katzenellenbogen, Tetrahedron Let., 1277 (1973), S. Bowlus and J. Katzenellenbogen, J. Org. Chem., **38**, 2733 (1973).