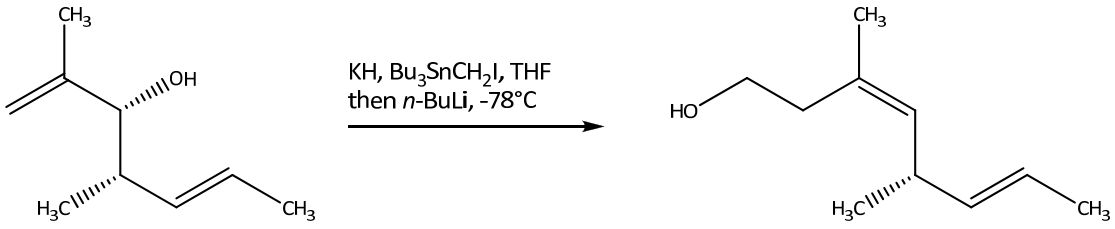
Written Qualifying Examinations
22 January 2008
Organic Chemistry

These questions are based on the following article:
Smith, Thomas E. et al. "Total Synthesis of (-)-Hennoxazole A". *J. Org. Chem.,* 73 (1), 142 -150, 2008.

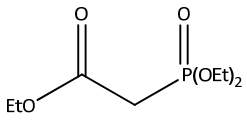
1. (3 points). The synthesis of the C_{16}-C_{25} side chain fragment begins with a [2,3]-Wittig-Still rearrangement, which provides homoallylic alcohol **37** as a single isomer. Propose a reasonable mechanism for this rearrangement and explain why only one stereoisomer is produced.



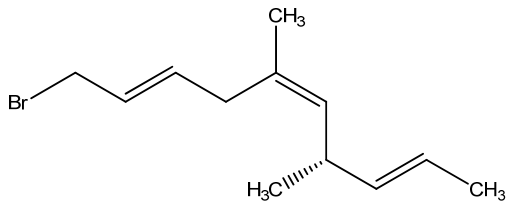
7 **37**

2. (1 point) What is Hünig's base? What is it commonly used for?

3. (3 points) Compound **37** above is then oxidized to the corresponding aldehyde, which is subjected to a Horner-Wadsworth-Emmons olefination. The reagent used in the olefination is shown below. What is the final product of the olefination? What is the mechanism leading to it?



4. (3 points) Compound 5, shown below, has the following spectral data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.75-5.67 (m,2H), 5.42-5.32 (m, 2H), 5.06 (d, J = 8.9 Hz, 1H), 4.00-3.92 (m, 2H), 3.03-2.95 (m, 1H), 2.82-2.74 (m,2H), 1.66 (d, J = 1.3 Hz, 3H), 1.64 (d, J = 4.5 Hz, 3H), 1.01 (d, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (125 MHz, CDCl3) δ 136.0, 133.8, 131.4, 131.0, 127.2, 122.8, 35.4, 34.9, 33.3, 23.5, 21.5, 18.0 ppm; IR (film) 2964, 2927, 2868, 156, 1438, 1377, 1203, 965, 854, 580 cm^{-1}; [α]D24 = –69.3° (c = 1.00, $CHCl_3$); HRMS (EI): Exact mass calcd for $C_{12}H_{19}Br$ [M]+: 242.0670; Found: 242.0663. The ^{1}H NMR is attached as a separate sheet of paper. Assign as many peaks in the ^{1}H NMR as you can.



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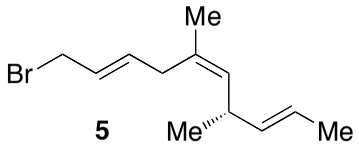
Green Chemistry Questions (2 points):

1. The conversion of compound **7** to compound **37** in one step in this synthesis replaces a six-step sequence in an earlier published synthesis of (-)-hennoxazole A. Would you say that the synthesis published in this paper is therefore "greener" than the earlier one? Why or why not? Which principle(s) of Green Chemistry would you invoke in your explanation? What other steps could be taken to improve the "greenness" of this synthesis? Be specific in your answer (suggested catalysts, solvent replacements, etc.).

2. Total syntheses of natural products tend to be very lengthy and often use many protecting groups that are then removed and essentially discarded. How does this practice affect the "greenness" of a proposed synthesis? Comment on the synthesis published in this paper from this perspective.



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^{1}HNMR: 500 MHz in $CDCl_3$