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THE EFFECT OF THE TRIMETHYLSILYL GROUP ON THE REGIOCHEMISTRY OF THE ENE REACTION

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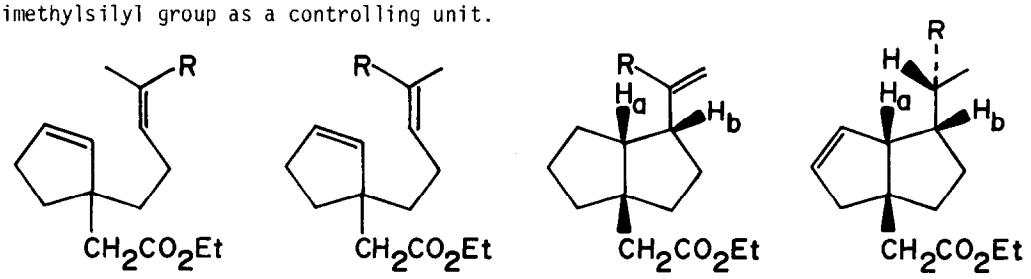
Abstract: The trimethylsilyl group has been found to have a profound effect on the regiochemistry of the ene reaction of E-1-methyl-2-trimethylsilyl olefins during the formation of [3.3.0] bicyclo-octanes.

Our interest in the tandem Claisen-ene rearrangement[1] and the desire to develop efficient methods for the control of both the regio- and stereochemistry of the ene reaction for eventual applications in organic synthesis led us to explore the role of the trimethylsilyl group as a controlling unit.



1 2 3 4

a, R=H; b, R=TMS

The four substrates, 1a, 2a, 1b, and 2b, were subjected to sealed tube thermolysis at 300°C in the presence of benzene-d_6. The product distributions are listed in the Table.

The results obtained in the rearrangement of 1a were not unexpected. Oppolzer has demonstrated that a trifluoroacetamide analog of 1a provides a 1:1 mixture of olefinic isomers. A coupling constant of J_{AB} = 8.0 Hz in 3a and 4a requires a cis arrangement of H_a and H_b.[3] In related tandem Claisen-ene rearrangements (1a, CO_2Et = $CONMe_2$ or CHO), both products afforded the same perhydro derivative upon hydrogenation, requiring the same relative stereochemistry in both 3a and 4a.[1] The olefin 2a exhibited only a moderate preference for the formation of isomer 3a over 4a.

Vinyl isomer 3a is formed through transition state A while its olefinic regioisomer 4a arises through transition state C.[4] Molecular models indicate that little change in

Table

Substrate	Conditions[a]	Products[b] 3a	4a	3b	4b
1a	15 h, quant 8h, 83% conv	1	1	-	-
2a	8h, quant	3	1	-	-
1b	14h, quant[c]	-	-	3 (1	2 1)[d]
2b	8h, quant	-	-	100	0

a) Yields were determined by ^{1}H NMR integration (90 MHz) of residual protiobenzene vs. vinyl hydrogens before and after thermolysis, b) all thermolysis products were purified by gas chromatography and identified by spectroscopic methods[2], c) minimum time for the disappearance of starting material, d) corrected for the presence of 20% of 2b in this sample.

transition state geometry would be required for the rearrangement to pass through either A or C. Transition state B, which would give rise to the side chain vinyl epimer of 3a, is of higher energy than A or C. For cis isomer 2a, transition state D leading to 3a is more favored than F, which gives 4a. No products derived from transition state E were detected.

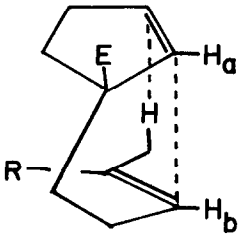
The exclusive formation of bicyclic vinylsilane 3b (J_{AB} = 7.9 Hz) from the E-(cis-Me) vinylsilane 2b requires transition state D (R = TMS) to be overwhelmingly more favorable than F (R = TMS) since the trimethylsilyl group of D is remote from steric interactions with ring hydrogens.

Z-(trans-Me) vinylsilane 1b provided a test as to whether or not the trimethylsilyl group would render transition states A and C unfavorable relative to B, which would place the trimethylsilyl group in an uncongested environment, but yet introduce strain in the transition state. This was found not to be the case since the bicyclic vinylsilane 3b, and not its side chain vinyl stereoisomer, was formed. Regioisomer 4b (J_{AB} = 7.6 Hz) (side chain stereochemistry inferred) must perforce arise through transition state C. Although transition states A and C encounter incipient interactions between the trimethylsilyl group and the ring, they provide a lower energy pathway than the strained trans-exo transition state of B.[5]

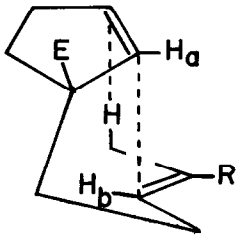
These results provide a potential method for controlling the regiochemical course of ene reactions in the formation of functionalized cis-fused [3.3.0] bicyclo-octanes.

Although vinylsilanes such as 3b are not readily protodesilylated or desilylated by fluoride ion when trimethylsilanes are employed, the use of phenyl substituted silanes holds promise for regenerating the vinyl group in the latter instance.[6]

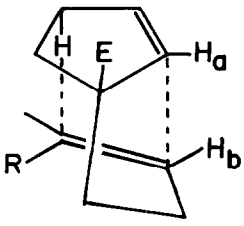
E = CH_2CO_2Et



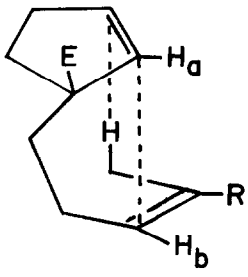
A: trans-endo



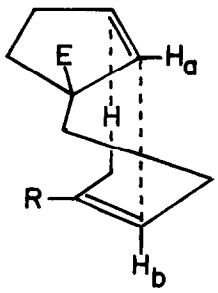
B: trans-exo



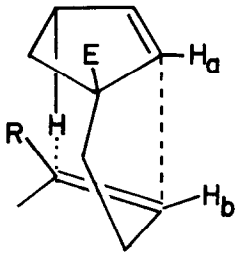
C: trans-regioisomeric



D: cis-exo



E: cis-endo



F: cis-regioisomeric

ACKNOWLEDGMENTS: This work was supported by NIH Grant GM29468. NMR spectra were recorded at the Northeast Regional NSF/NMR Facility at Yale University, which is supported by grant CHE-7916210 from the Chemistry Division of the National Science Foundation.

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2. The substrates 1a, 1b, and 2b were prepared by orthoester Claisen rearrangement of the appropriate cyclopentenols which were in turn prepared by $LiAlH_4$ reduction of the 3-alkylcyclopentenones. The latter substances were produced by addition of the appropriate side chain Grignard reagent to 3-methoxycyclopentenone. Z-4-trimethyl-

silyl-4-penten-1-ol was prepared by the hydromagnesiation-alkylation procedure of Sato.[7] The E-isomeric alcohol was prepared as described.[8] The bromides were prepared from the alcohols by sequential treatment with MsCl/Et_3N (CH_2Cl_2, -50°C, 15 min) and LiBr/THF (25°C, 18h). Ester 2a was prepared by protrodesilylation of 2b (C_6H_6, I_2). 1a: NMR (270 MHz) δ 1.25 (t, J = 7.2 Hz, 3H), 1.40-2.40(m, 8H), 1.63(dd, J = 3.3, 1.2 Hz, 3H), 2.37(s, 2H), 4.11(q, H, J = 7.2 Hz, 2H), 5.38(m, 2H), 5.60(m, 1H), 5.71(m, 1H); 2a: NMR (270 MHz) δ 1.25(t, J = 7.2 Hz, 3H), 1.40-2.40(m, 8H), 1.60(d, J = 5.1 Hz, 3H), 2.39(s, 2H), 4.11(q, J = 7.2 Hz, 2H), 5.39(m, 2H), 5.62(m, 1H), 5.72(m, 1H); 1b: NMR (270 MHz) δ 0.10(s, 9H), 1.26(t, J = 7.1 Hz, 3H), 1.75(d, J = 1.7 Hz, 3H), 1.50-2.40(m, 8H), 2.40(s, 2H), 4.12(q, J = 7.1 Hz, 2H), 5.62(m, 1H), 5.73(m, 1H), 5.91(t, J = 6.3 Hz, 1H); 2b: NMR (270 MHz) δ 0.03(s, 9H), 1.25(t, J = 7.1 Hz, 3H), 1.65(d, J = 1.7 Hz, 3H), 1.50-2.40(m, 8H), 2.40(s, 2H), 4.12(q, J = 7.1 Hz, 2H), 5.58-5.78(m, 3H); 3a: NMR (270 MHz) δ 1.27(t, J = 7.2 Hz, 3H), 1.00-2.00(m, 10H), 2.17(q, J = 8.0 Hz, 1H), 2.35(d, J = 13.5 Hz, 1H), 2.42(d, J = 13.5 Hz, 1H), 2.55(m, 1H), 4.14(q, J_{AB} = 7.2 Hz, 2H) 4.15(q, J_{AB} = 7.2 Hz, 2H), 4.92(br. d, J = 10.3 Hz, 1H), 5.0(br. d, J = 17.6 Hz, 1H), 5.87(d,d,d, J = 17.6, 10.3, 6.5 Hz, 1H); 4a: NMR (270 MHz) δ 0.93(t, J = 7.3 Hz, 3H), 1.27(t, J = 7.2 Hz, 3H), 1.00-2.00(m, 7H), 2.26(d,d,d, J = 17.4, 5.2, 2.3 Hz, 1H), 2.47(s, 2H), 2.57(d,d,d, J = 17.4, 5.4, 2.2 Hz, 1H), 2.87(br. d, J = 8.0 Hz, 1H), 4.13(q, J = 7.2 Hz, 2H), 5.50(m, 1H), 5.64(m, 1H); 3b: NMR (270 MHz) δ 0.10(s, 9H), 1.28(t, J = 7.2 Hz, 3H), 1.00-2.00(m, 10 H), 2.18(q, J = 7.9 Hz, 1H), 2.38(d, J_{AB}= 13.8 Hz, 1H), 2.45(d, J_{AB} = 13.8 Hz, 1H), 2.70(m, 1H), 4.14(q, J = 7.2 Hz, 1H), 4.15(q, J = 7.2 Hz, 1H), 5.42(m, 1H), 5.56(m, 1H); 4b: NMR (270 MHz) δ 0.08(s, 9H), 1.00(d, J = 7.3 Hz, 3H), 1.26(t, J = 7.1 Hz, 3H), 1.00-1.80(m, 6H), 2.28(d,d,d, J = 17.4, 5.2, 2.3 Hz, 1H), 2.47(s, 2H), 2.60(d,d,d, J = 17.4, 5.4, 2.2 Hz, 1H), 3.02(br. d., J = 7.6 Hz, 1H), 4.13(q, J = 7.1 Hz, 2H), 5.56(m, 1H), 5.69(m, 1H).

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