Tetrahedron Letters,Vol.25,No.44,pp 5067-5070,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

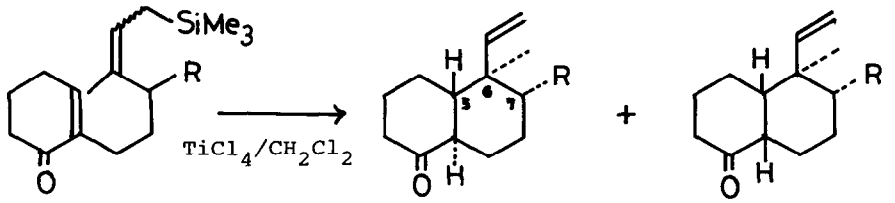
REMARKABLE STEREOCONTROL OBSERVED IN THE RING FORMATION BY INTRAMOLECULAR HOSOMI-SAKURAI REACTION[1]

Takashi Tokoroyama,* Masamitsu Tsukamoto, and Hideo Iio
Faculty of Science, Osaka City University, Sumiyoshi-ku, Osaka 558, Japan

Summary: The cyclization of 2-(3',4'-dimethyl-6'-trimethylsilyl-4'-hexenyl)-2-cyclohexenone with $TiCl_4$ afforded stereospecifically 6α,7α-dimethyl-6β-vinyl-5βH-1-decalone derivative and the two-fold diastereoselection involved is reasoned in terms of orientation control and folding strain control.

Stereocontrol in ring formation is a key problem for the synthesis of cyclic natural products. Aside from the Diels-Alder reaction, there are few methods, by which the stereoselectivity at several asymmetric centers are secured at the same time. We delineate here a distinct diastereoselection at three contiguous carbon atoms (practically four, vide infra) in the cyclization by means of the intramolecular Hosomi-Sakurai reaction.[2]

In connection with the synthetic studies on clerodane diterpenoids,[3,4] we concerned with the stereospecific construction of 6α,7α-dimethyl-6β-substituted 5βH-1-decalone and investigated the cyclization reaction based on an allylsilane strategy as shown in Scheme 1.[5] We envisaged that the diastereocontrol at C-7 relative to C-5 might be possible to some degree in addition to that at C-6. Firstly the cyclization of 2-(4'-methyl-6'-trimethylsilyl-4'-hexenyl)-2-cyclohexenone 1 was examined in order to study the diastereoselectivity with respect to C-5 and C-6. The substrate allylsilane 1 was prepared as depicted in Scheme 2. 2-(4'-Oxopentyl)-2-cyclohexenone 8 obtained by the method of A. B. Smith, III[6] was treated with 2-trimethylsilylethylidene triphenylphosphorane[7] to afford regioselectively 1 (E/Z = 3:2) in 40% yield with the intramolecular Michael product 9 (30%). The reaction of 1 with $TiCl_4$ in CH_2Cl_2 at -78 °C proceeded smoothly giving two cyclized products 2 and 3 (3:2 ratio)[8] in 90% yield. Since 3 was converted quantitatively to 2 in equilibrium condition



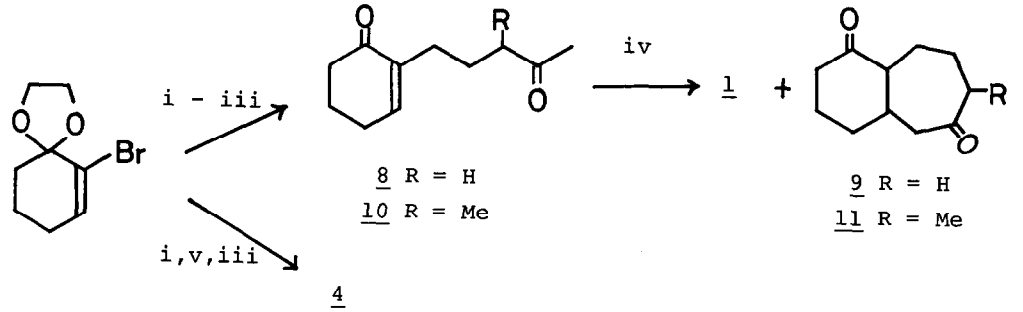
1 R = H
4 R = Me

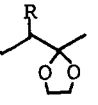
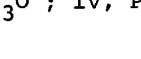
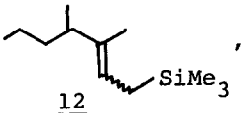
2 R = H
5 R = Me

3 R = H
6 R = Me

Scheme 1

(MeONa/MeOH), both compounds represent the isomers of the ring junction, cis and trans respectively, and the fact signify the diastereoselection with respect to C-5 and C-6 are essentially complete independent of the double bond geometry in the allylsilane chains. The relative configuration at C-5 and C-6 was assigned as indicated from ^{13}C NMR chemical shift difference of 6-methyl carbon atoms[9] and a chemical conversion.[10]

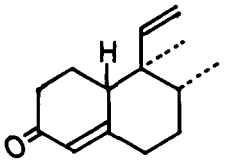


Scheme 2: i, n-BuLi; ii,  , HMPA; iii, H_3O^+; iv,  ; v,  , HMPA

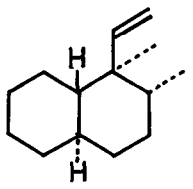
12

Encouraged by the promising preliminary result, we proceeded to the cyclization study of 2-(3',4'-dimethyl-6-trimethylsilyl-4'-hexenyl)-2-cyclohexenone 4. The synthesis of 4 in the same way as for 1 failed since treatment of the diketone 10 with the Wittig reagent resulted in the exclusive formation of 11. Eventually 4 (E/Z = 5:4) was synthesized by the combination of the cyclohexenone moiety with the preformed allylsilane side chain[11] in the same way as 8 (Scheme 2). The cyclization of 4 in the same condition above afforded a mixture (3:1 ∿ 4:1 ratio) of trans and cis decalones 5 and 6[12] in 80% yield, the treatment of 6 with MeONa/MeOH at room temperature giving 5. The configuration of 5 as shown in the formula (desired for the synthesis of the natural products !) has been confirmed by the chemical correlation to the octalone derivative 13 with the established configuration.[4] Thus trans decalin 14 obtained by the Wolff-Kischner reduction of 5 was found to be identical with the compound derived from 13 through consecutive reductions with Li/NH_3 and the Wolff-Kischner procedure. Consequently it turns out that the splendid diastereocontrols are operative not only at C-5 and C-6 but also at C-7 during the cyclization.

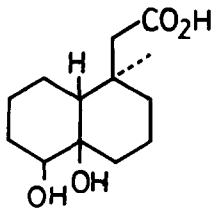
The two-fold diastereoselection achieved in the cyclization of 4 are rationalized by the consideration of two kinds of stereocontrol imposed in the transition state. First let us examine the cyclization of 1, where a diastereomeric C-C bond formation is involved. Provided that chair-like conformation of the emerging ring in the transition state is preferred to the boat-like one,



13

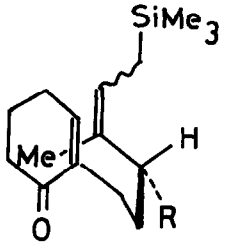


14

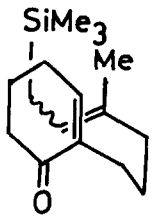


17

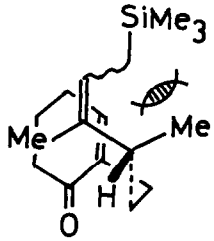
two types of ring formation, 15a and 15b are discriminated with respect to the orientation of the allylsilane group to the cyclohexenone ring (exo and endo). Of these the exo-attack 15a leading to the observed stereoselection would be favored from the view of steric repulsion and/or stereoelectronic effect[13] (orientation control) and the situation would not be substantially changed by the geometry of the allylsilane double bond. Next in the cyclization of 4, two types of chair-exo transition state 16a and 16b are taken into account with reference to the conformation of 7-methyl group. When we take notice of the $A^{1,3}$ interaction[14] present in 16b,[15] the transition state 16a should be energetically favored and the observed stereospecificity is aptly explained. Thus the second stereocontrol originated from the energy difference in the folding of the allylsilane side chain leading to the transition state and may be termed as folding strain control.[16]



15a R = H
16a R = Me



15b



16b

The studies to explore the scope of the stereocontrol in the allylsilane cyclization as well as the synthesis of the natural product by the methodology described are being under way.

References and Notes.

1. Synthetic Studies on Terpenic Compounds XVII. For part XVI, see ref. 4.
2. A. Hosomi and H. Sakurai, J. Am. Chem. Soc., 99, 1673 (1977).
3. T. Tokoroyama, K. Matsuo, and T. Kubota, Tetrahedron, 34, 1907 (1978).
4. T. Tokoroyama, K. Fujimori, T. Shimizu, Y. Yamagiwa, M. Monden, and H. Iio, J. Chem. Soc., Chem. Commun., 1516 (1983).
5. There appear only a few reports on the ring formation which utilize the intramolecular reaction between allylsilane and α,β-unsaturated carbonyl group: (a) S. R. Wilson and M. F. Price, J. Am. Chem. Soc., 104, 1124 (1982) ; (b) G. Majetich, R. Desmond, and A. M. Casares, Tetrahedron Lett., 24,

1913 (1983).
6. M. A. Guaciaro, P. M. Wovkulich, and A. B. Smith, III, Tetrahedron Lett., 4661 (1978).
7. D. Seyferth, K. R. Wursthorn, and R. E. Mammarella, J. Org. Chem., 42, 3104 (1977); I. Flemming and Paterson, Synthesis, 446 (1979).
8. The assigned structures are supported from spectral data. 2: IR($CHCl_3$), 1705, 910 cm^{-1}; ^1H NMR($CDCl_3$), 1.04 (3H, s), 4.60 ∿ 6.00 (3H, ABX system with J_{AB} = 2, J_{AX} =18, J_{BX} = 10 Hz); ^{13}C NMR($CDCl_3$), 213.3(s), 149.1(d), 111.4(t), 50.9(d), 49.8(d), 42.1(t), 40.2(s), 39.5(t), 26.5(t), 26.3(t), 25.6(t), 20.5(t), 15.6(q); 3: ^1H NMR, 0.95 (3H, s), 4.77 ∿ 6.00 (3H, ABX system); ^{13}C NMR, 215.3(s), 147.1(d), 112.4(t), 50.2(d), 45.7(d), 38.8(s), 37.7(t), 32.3(t), 28.4(q), 25.5(t), 24.9(t), 21.5(t), 20.7(t).
9. R. Beier, Org. Mag. Res., 11, 586 (1978); I. Salasoo, Phytochemistry, 23, 192 (1984).
10. The glycol 17 derived from 2 by the following sequence of the reactions was found to lactonize spontaneously during workingup: (i) ethylene glycol/CSA; (ii) B_2H_6/THF; (iii) $RuCl_3/NaIO_4$; (iv) H_3O^+; (v) $TsNHNH_2$; (vi) Na/ethylene glycol; (vii) OsO_4/pyridine; (viii) Na_2SO_3/H_2O/EtOH. This fact indicates that the bridge-head hydrogen and the carboxymethylene group are juxtaposed in the same side of the molecule since the attack of OsO_4 is known to occur from the convex side of the educt Δ^4-octalone.[3]
11. The compound 12 was prepared from tiglic aldehyde by the sequence of the reactions including the Claisen rearrangement[5a]: (i) $ClMgCH_2SiMe_3$; (ii) CH_2=CHOEt/$Hg(OAc)_2/\Delta$; (iii) $NaBH_4$; (iv) MsCl/Et_3N; (v) NaI/DMF.
12. 5: ^1H NMR, 0.74 (3H, d, J = 7 Hz), 0.90 (3H, s), 4.87 (1H, dd, J = 2,17 Hz), 5.03 (1H, dd, 2,11 Hz), 5.42 (1H, dd, J = 11,17 Hz); ^{13}C NMR, 213.5(s), 147.9(d), 113.3(t), 51.8(d), 49.4(d), 44.3(s), 42.0(t), 39.9(d), 28.7(t), 26.4(t), 26.1(t), 25.6(t). 16.6(q), 9.0(q).
13. Preference of the linear or extended transition state is assumed for aldol and the related reactions. See R. Noyori, I. Nishida, and J. Sakata, J. Am. Chem. Soc., 103, 2106 (1981); Y. Yamamoto, H. Yatagi, Y. Narita, and K. Maruyama, ibid., 102, 7107 (1980); T. Hayashi, M. Konishi, and M. Kumada, ibid., 104, 4963 (1982). See also T. A. Blumenkopf and C. H. Heathcock, ibid., 105, 2354 (1983).
14. F. Johnson and S. K. Malhotra, J. Am. Chem. Soc., 87, 5492 (1965); F. Johnson, Chem. Rev., 68, 375 (1968).
15. The inspection of molecular model reveals that this interaction exists between the trimethylsilylmethylene group (Z isomer) or the hydrogen atom (E isomer) and proaxial substituent at C'-3 rather than proequatorial one due to the rotation about C'-3-C'-4 bond for the effective overlapping of the π-systems. It would be greater in the Z than E isomers, but still in the latter could be enough for the control of the steric pathways.
16. The term applies to the stereocontrol in the cyclization which exerts at diastereotopic atoms other than those concerning with the bond formation and the strain involved could be of all kinds (tortion strain, nonbonded interactions, and dipolar interaction etc.). In principle the folding strain control could be operative in various types of the cyclization reaction[17] and also in acyclic reactions which comprise cyclic transition state. In fact it has common features in many respects with acyclic control.
17. For example the concept is implicitly expressed in the stereocontrol of an intramolecular Diels-Alder reaction: M. Yoshioka, H. Nakai, and M. Ohno, J. Am. Chem. Soc., 106, 1133 (1984). See also G. Brieger and J. N. Bennett, Chem. Rev., 80, 63 (1980).

(Received in Japan 9 July 1984)