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X-RAY STRUCTURE OF A CHIRAL ALKENE: DIRECT EVIDENCE FOR C-H BOND ECLIPSING C=C BOND

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Abstract: A single crystal X-ray structure determination of the chiral alkene, (1Z)-1-(benzyloxymethyloxy)-3-cyclohexyl-4-phenyl-1-buten-4-ol, (**1**), is described. The observed conformation about the C_{sp2}-C_{sp3} bond of **1** is the C-H eclipsed form in the crystal and in solution.The observed torsional angles in the acetal portion of the structure are -65° for R'-O-C-O and -59° for O-C-O-R".

The conformational behavior of allylic compounds has direct consequences on their reactivity. During the last three decades, considerable effort has been devoted to the understanding of the conformational profiles of allylic substrates. It is accepted that the three rotamers with the allylic C-X (or C-H) bond eclipsing the C=C bond are the energy minima on the Csp3-Csp2 rotational profile.[1] Bothner-By[2] and coworkers have determined the free energy differences between the two eclipsed rotamers of 3-substituted alkenes. The C-X eclipsed form (X = F, MeO) was found to be the more stable conformation for allyl fluoride, and allyl methyl ether by 100, and 115 cal/mol respectively; and the C-H eclipsed form was found to be the more stable conformer for allyl chloride, bromide, and iodide by 100, >500, and >>2000 cal/mol respectively.

The conformational preference of chiral alkenes has been shown to play an important role in asymmetric reactions. However, few reports involving direct experimental determination of chiral alkene conformations have appeared.[3,4] Through a study of the CD spectra of chiral allylic *p*-bromobenzoates, Nakanishi and Sharpless[3] and their coworkers have determined that the C-H eclipsed rotamer is predominant among the possible conformations. Wilson[4] et al. have conducted a microwave spectroscopic study of 3-buten-2-ol. The C-H eclipsed form was found to be about 500 cal/mol more stable than the C-O eclipsed form. Conformation with C-C bond eclipsing the C=C bond was not detected. We wish to report the first X-ray structure of a chiral alkene. The preparation of **1** is depicted in Scheme I.

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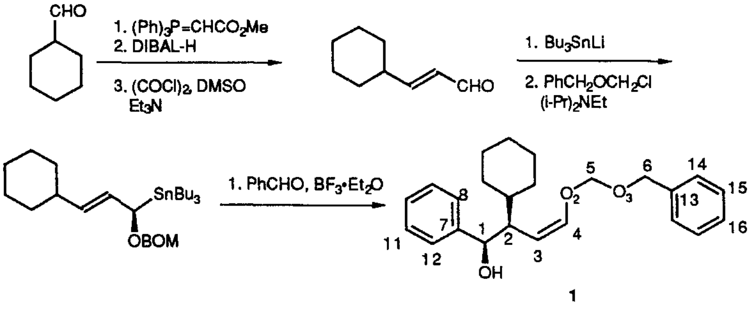
Scheme I



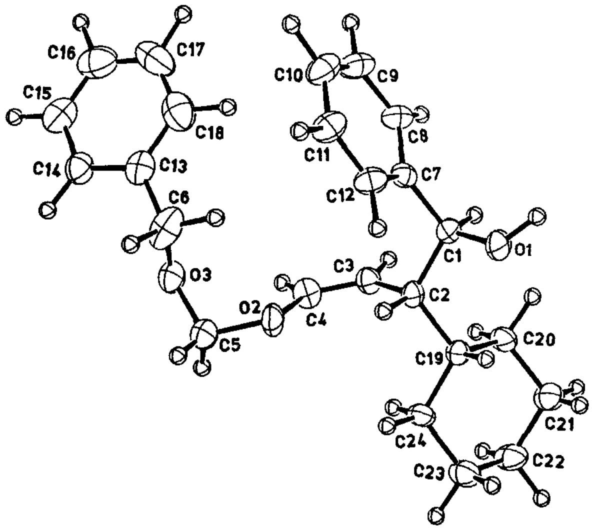


Figure 1 The ORTEP[14] drawing of the structure of **1** from a single crystal X-ray analysis.

The ORTEP drawing of the structure of **1** is shown in **Figure 1**.

The preferred conformation around the C_{sp2}-C_{sp3} bond assumes the C-H eclipsed form. However, the eclipsing is not perfect. The torsional angle (H2-C2-C3-C4) is 7.2 degree. This is consistent with the asymmetric structure of a chiral molecule. Theoretical calculations by *ab initio* MO methods have shown that chiral allylic alcohols and ethers have the C_{sp2}-C_{sp3} torsional angles about 10° from the eclipsed form.[5] The microwave spectroscopic study of 3-buten-2-ol has also shown a 2 to 4 ° deviation from the complete eclipsed forms.[4] For the current case, an apparent cause that the alternative C-C eclipsed forms are disfavored is the (Z) configuration of the double bond. The conformational preference in (Z) chiral alkenes has been invoked as the primary cause for their excellent π-facial selectivity.[6] The so called allylic 1,3-strain in relation to asymmetric induction has been reviewed.[7] The proton coupling constant $^3J_{2,3}$ of **1** is 11.3 Hz in chloroform at room temperature. By applying the Karplus[8] type of equation developed especially for Csp2-Csp3 rotamer

$$\begin{aligned} ^3J_{est} &= 6.6\cos^2\phi + 2.6\sin^2\phi \ (0° < \phi < 90°) \\ ^3J_{est} &= 11.6\cos^2\phi + 2.6\sin^2\phi \ (90° < \phi < 180°) \end{aligned} \qquad (1)$$

by Garbish, eq. (1),[9] a maximum of 11.6 Hz can be calculated for the complete eclipsed form. Therefore, a coupling constant of 11.3 Hz indicates that the population of the C-H eclipsed rotamer is overwhelming even in solution at room temperature. Thus, our observation confirms the recent theoretical study[10] which has shown that for (Z)-4-methyl-2-pentene, there is only one stable conformation on the Csp2-Csp3 rotational profile.

The second interesting feature of the structure is the acetal portion of the molecule. The torsional angles for C6-O3-C5-O2 and O3-C5-O2-C4 are -65° and -59° respectively. This is the one conformation (out of six possible isomers) that Deslongchamps[11] et. al. has predicted based on kinetic studies of the ozonalysis of acyclic and cyclic acetals and corroborated by theoretical investigations.[12] In addition to this apparent manifestation of anomeric effect, another observation is the shortening of the C6-C13 bond length. Although of exactly the same bonding type (C_{sp2}-C_{sp3}), the two bonds C1-C7 (1.524 Å) and C6-C13 (1.481 Å) are considerably different. Apparently, a vinyl-analogous anomeric effect, i.e. $\pi \rightarrow \sigma^*_{C\text{-}O}$, is operating.[13] The nearly perpendicular dihedral angle between the phenyl ring and C6-O3 testifies to this effect since the *p* orbital on C13 can interact with the antibonding orbital σ*C6-O3 in this conformation.

X-ray Crystallographic Analysis of 1. $C_{24}H_{30}O_3$, monoclinic, space group $P2_1/c$, a = 14.956 (2), b = 6.098 (2), c = 24.382 (5) Å, β = 109.03(2)°, Z = 4, MW = 366.5 g/mol, D_c = 1.16 g/cm^3. A clear colorless prismatic crystal (0.11 x 0.20 x 0.56 mm) which showed sharp optical extinction under crossed polarizers was selected form a batch of crystals grown from a mixed hexane/ether solution. Unit cell parameters and intensity data were measured using Mo K radiation (λ = 0.71069 Å) at 290 K on an Enraf-Nonius X-ray diffractometer equipped with a graphite monochromator. Three control reflections monitored every 250 measurements showed no significant variation in intensity. The total number of unique reflections collected was 2422. Of these, 1621 had $F_o > 2\sigma(F_o)$ and were used in the structure analysis. Absorption and extinction corrections were not applied. The structure was solved using a combination of direct and difference Fourier methods and refined (244 variable parameters) by a full-matrix least-squares procedure. Programs used include the Enraf-Nonius SDP-Plus program package running on IBM 4381 and VAX 6000 computers. Hydrogen atom parameters were included in the structure factor calculations but were not refined. Anisotropic refinement for all nonhydrogen atoms converged to R = 0.091, R_w = 0.069 and GOF=1.51. The weighting scheme used was: $w = [\sigma(F_o)^2 + (0.02F_o)^2]^{-1}$, where $\sigma(F_o)$ was obtained from counting statistics. Maximum shift/e.s.d. for any parameter in the final least-squares refinement was 0.01. A final difference Fourier showed no significant residual electron density.

In summary, we have described a crystallographic analysis of a chiral alkene. First direct experimental evidence is observed for 1,3-allylic strain. In the crystal or in solution, compound **1** exists predominantly in nearly C-H eclipsed forms. Experiments designed to determine the conformational profiles of various chiral alkenes are underway in our laboratories.

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