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Transition States for the Hydrogen Atom Abstraction Reaction by α-Oxygen Substituted Radicals: Felkin-Anh Rule in Radical Chemistry

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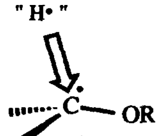
Key Words: stereochemistry; radicals; ab initio calculations; transition states; conformational analysis; ESR-spectroscopy

Abstract: *Ab initio calculations on transition states of the hydrogen atom abstration by α-oxygen substituted radicals show that the Felkin-Anh rule can be applied to radical chemistry.*

Recently, Giese and Curran et al. have shown that Cram's rule can be applied to radical chemistry.[1] We concluded that the transition state of hydrogen atom abstraction with oxygen substituted radicals **1** resembles the Felkin-Anh transition state **2** of ionic reactions. An important feature of the Felkin-Anh[2] transition state is the nearly tetrahedral angle of attack between the developing C,H-bond and the C,O-bond of the carbonyl group.[3] To see whether in radical hydrogen atom abstraction the angle of attack is also non-perpendicular, we calculated the transition structures for the reactions of siloxyalkyl radicals **3a-c** with silane as the hydrogen atom donor.[4]



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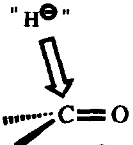

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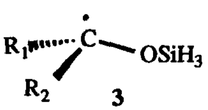

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a: $R_1 = R_2 = H$
b: $R_1 = H$, $R_2 = CH_3$
c: $R_1 = R_2 = CH_3$

The transition structures **4-6** demonstrate that the angle of attack in the radical hydrogen atom abstraction is already tetrahedral (α=108-109°). It is remarkable that this angle is nearly independent on the bulk of the substituteds R^1 and R^2. Thus, the non-perpendicular attack seems to be typical for reactions of the oxygen substituted radicals (Fig. 1).[5]

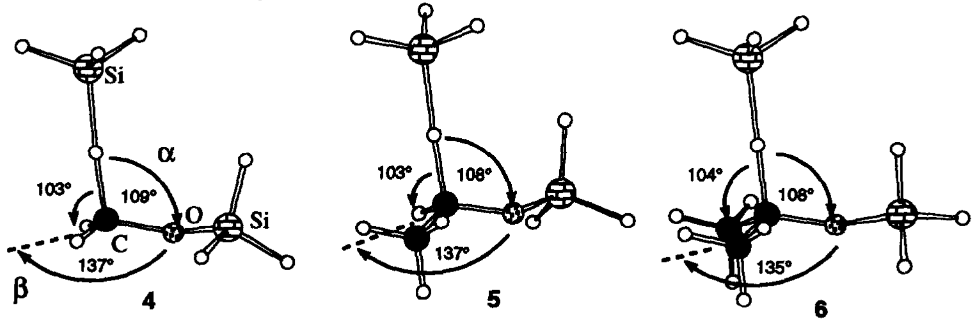


Figure 1. UHF/6-31G* optimized transition structures are shown for **4**, **5** and **6**.

The radical centers in transition states 4-6 are bent to a considerable degree (β=135-137°). This is not surprising, because oxygen-substituted radicals are pyramidal already in the ground state.[6] For radicals **7a,b** we proved this bending by measuring the ^{13}C-ESR coupling (Fig. 2).[7] The coupling constants of 61.9 and 61.4 Gauss, respectively, show that these radicals are already pyramidal.[6] The calculated angle of deformation in radical **7a** is 144°(β, Fig. 1).[4]

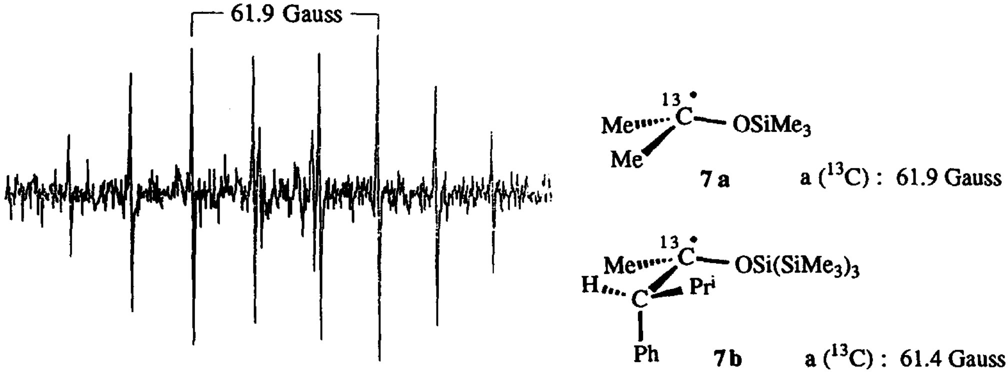
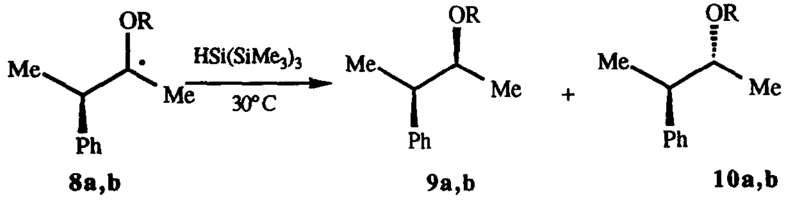


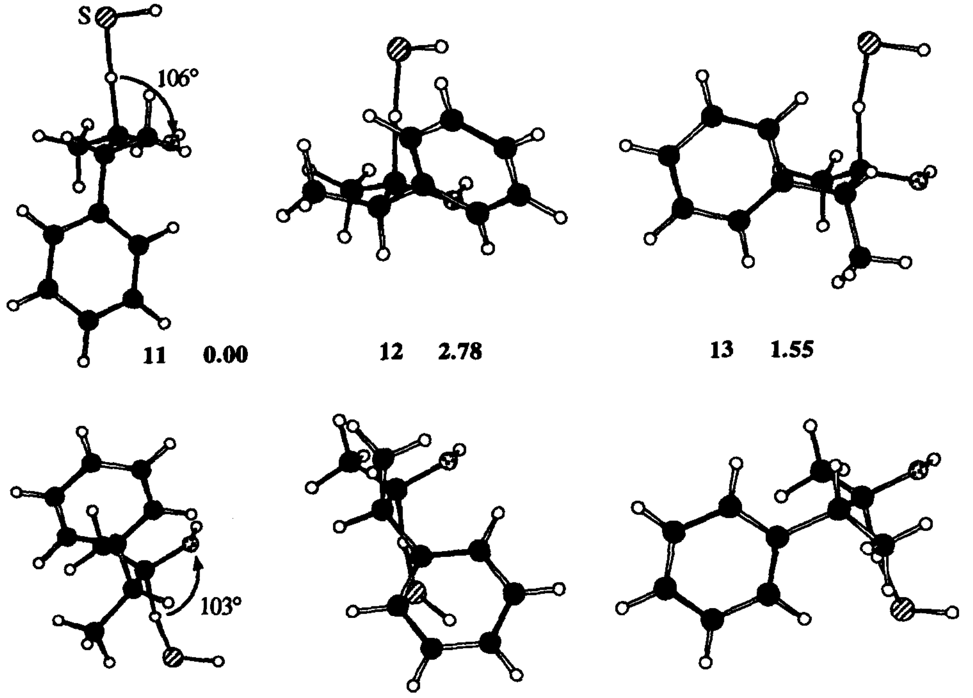
Figure 2. ESR spectrum of the ^{13}C -labeled compound 7a (-40°C).

In order to see whether a chiral substituent at the radical center prefers a Felkin-Anh conformation[2] we optimized the transition structures for chiral radical **8a**, because the analogous silylated radical **8b** reacts stereoselectively and gives **9b** as the major product.[1] For each of the two directions of attack three transition structures with different orientations of the groups at the stereocenter were calculated with the PMP2/6-31G*//UHF/3-21G method (Fig. 3).[8]



a : R = H
b : R = $Si(SiMe_3)_3$ 75 : 25

From these transition structures (**11-16**) a stereoselectivity **9a** : **10a** = 73 : 27 (30°) was calculated. This is in good agreement of the observed selectivity (**9b** : **10b** = 75 : 25, 30°).[1]

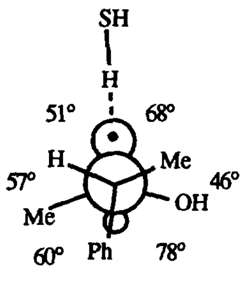


11 **0.00** **12** **2.78** **13** **1.55**

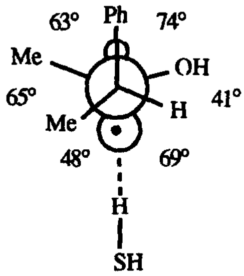
14 **1.69** **15** **1.64** **16** **0.67**

Figure 3. The top row shows the UHF/3-21G optimized structures with the hydrogen transfer from above. The bottom row shows the attack from below. Relative energies from the PMP2/6-31G* single point calculation are given in kcal/mol.

In the lowest energy structure, **11**, the chiral group at the radical center adopts a conformation in which the phenyl is nearly orthogonal to the C,O bond (dihedral angle=78°). The hydrogen atom donor is closer to the tertiary hydrogen atom (dihedral angle=51°, H/H-distance=246pm) than to the methyl substituent (dihedral angle=68°, H/C-distance=292pm) of the chiral group. Conformation **14**, in which the phenyl group shields the opposite face is 1.7 kcal/mol higher in energy than transition structure **11**, because the hydrogen donor comes closer to the methyl group of the chiral center (dihedral angle=48°, H/C-distance=277pm).[9]



11



14

Conclusion: The angle of attack (α, Fig. 1) on oxygen substituted radical is nearly tetrahedral. This leads to smaller steric repulsions in Felkin-Anh transion state compared to *anti*-Felkin-Anh conformations.

A detailed comparison between radical and ionic transition structures for related reactions are given by Prof. Houk and J. E. Eksterowicz.[10]

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