Pergamon

Tetrahedron 54 (1998) 5417–5422

TETRAHEDRON

Cyclic vs. Acyclic Allylic Hydrogen Abstraction: an Entropy Motivated Process?

Gadi Rothenberg and Yoel Sasson*

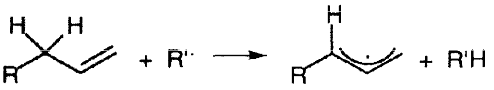
Casali Institute of Applied Chemistry, Hebrew University of Jerusalem, Jerusalem 91904, Israel.
e-mail: ysasson@vms.huji.ac.il

Received 20 February 1998; accepted 5 March 1998

Abstract: Optimized geometries for the reactants, products, and transition structures of cyclic and acyclic allylic hydrogen abstractions by *tert*-butoxy radicals were obtained by semiempirical methods. In the four model cases studied the transition structures were all early and linear, with large imaginary frequencies, around 2000 cm^{-1}. Enthalpic effects, rather than entropic ones, are deemed as responsible for the "cyclic activation" of allylic hydrogens towards free-radicals.

INTRODUCTION

The abstraction of allylic hydrogens by free-radicals is the rate-determining step in many allylic oxidations. As such, it is an important reaction in several fields, including industrial oxidations and natural product synthesis.[1, 2] In comparison with saturated hydrocarbons, hydrogen abstraction (HA) at allylic positions is facile, reflecting the resonance stabilization gained in the formation of the allylic radical (eq 1).

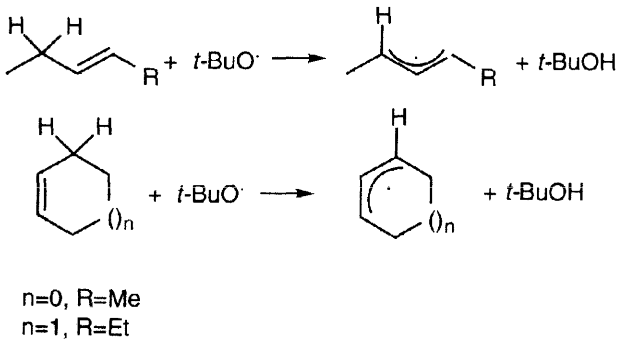


(1)

In papers dealing with HA processes, an enhanced reactivity of cyclic allylic substrates compared to acyclic ones is reported.[3] This factor is common to several systems, regardless of the abstracting species, and is not observed in the corresponding saturated compounds, so it cannot be due "simply" to differences in bond energies.[4-8] One explanation has attributed this "cyclic activation" phenomenon to entropy differences.[9] It has been argued that the acyclic molecule loses more entropy than its cyclic counterpart as the transition state (TS) is reached, assuming that the activated complex is similar to the incipient planar allylic radical.[10] One hypothesis, therefore, is that $k_{HA,cyclic}>k_{HA,acyclic}$ because $|\Delta S^{\ddagger}_{cyclic}|<|\Delta S^{\ddagger}_{acyclic}|$.[11, 12] Conversely, Ingold *et al* have proposed that this enhanced reactivity of cyclic structures is due to a combination of resonance, polar, and steric effects, rather than to one overriding process.[6, 13]

Recently we have shown that radical-π interactions, caused by alignment of the allylic hydrogen and the double bond on the same plane, can account for the regioselective allylic HA from 3-carene and α-pinene.[14] During this study, we were interested whether molecular modeling of the TS could predict the magnitude, and perhaps provide an explanation to the nature of the cyclic activation effect. The case chosen was the reaction originally studied by Walling and Thaler,[7] *viz.* the allylic HA by the *tert*-butoxy radical from cyclohexene vs. 3-hexene and cyclopentene vs. 2-pentene (eq 2 and 3).

0040-4020/98/$19.00 © 1998 Elsevier Science Ltd. All rights reserved.
PII: S0040-4020(98)00215-4



(2)

(3)

RESULTS AND DISCUSSION

The calculated thermodynamical parameters for the reactants, transition structures, and products are presented in tables 1 and 2. All computations were performed at the semiempirical level.

Table 1. Calculated Thermodynamical Parameters for Allylic HA (eq 2 and 3).

		ΔH^0_f (kcal/mol)			S^0 (cal/molK)			ΔH^0_r
Entry	Substrate	reactants	TS	products	reactants	TS	products	kcal/mol
1	cyclohexene	-31.1	-17.6	-64.5	54.3	43.9	34.6	-33.4
2	3-hexene	-37.4	-22.7	-70.5	41.6	36.1	42.8	-37.4
3	cyclopentene	-17.7	-3.7	-48.7	50.5	26.3	31.7	-17.7
4	2-pentene	-29.7	-14.9	-61.9	60.1	50.2	36.5	-29.7

Table 2. Activation Parameters[a] for Allylic HA (eq 2 and 3).

Entry	Substrate	$\Delta S^\ddagger$ cal/molK	$\Delta H^\ddagger$ kcal/mol	E_a kcal/mol[b]	TS Freq. cm^{-1}
1	cyclohexene	-10.4	13.6	14.2	-2184
2	3-hexene	-5.5	14.7	15.3	-1676
3	cyclopentene	-24.3	14.0	14.6	-1706
4	2-pentene	-9.9	14.8	15.4	-2116

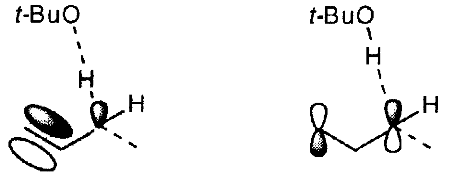
[a] Calculations pertain to 298.15 K. [b] $E_a \approx \Delta H^\ddagger + RT$.[15]

Entropy vs. enthalpy effects

Surprisingly, the computed values of $\Delta S^\ddagger$ do not support the traditional entropy-motivated explanation. On the contrary, a prediction based solely on these $\Delta S^\ddagger$ values, would have assigned a higher reactivity for the *acyclic* molecules! An alternative explanation to these findings can be based on the respective E_a values. Experimental results put $k_{HA,cyclic}/k_{HA,acyclic}$ between 4 and 6 (at 313 K).[7, 16] If we assume that $\Delta S^\ddagger$ does not contribute significantly to k, we can disregard the difference between the Arrhenius pre-exponential factors, and obtain $E_{a,cyclic} = E_{a,acyclic} - RT\ln Q$ (where $4 \leq Q \leq 6$). At 313 K, RTlnQ would equal 0.9 to 1.1 kcal/mol, which is quite comparable with our calculated values of ΔE_a (1.1 and 0.8 kcal/mol for cyclohexene/3-hexene and cyclopentene/2-pentene, respectively).

Characteristics of the transition state.

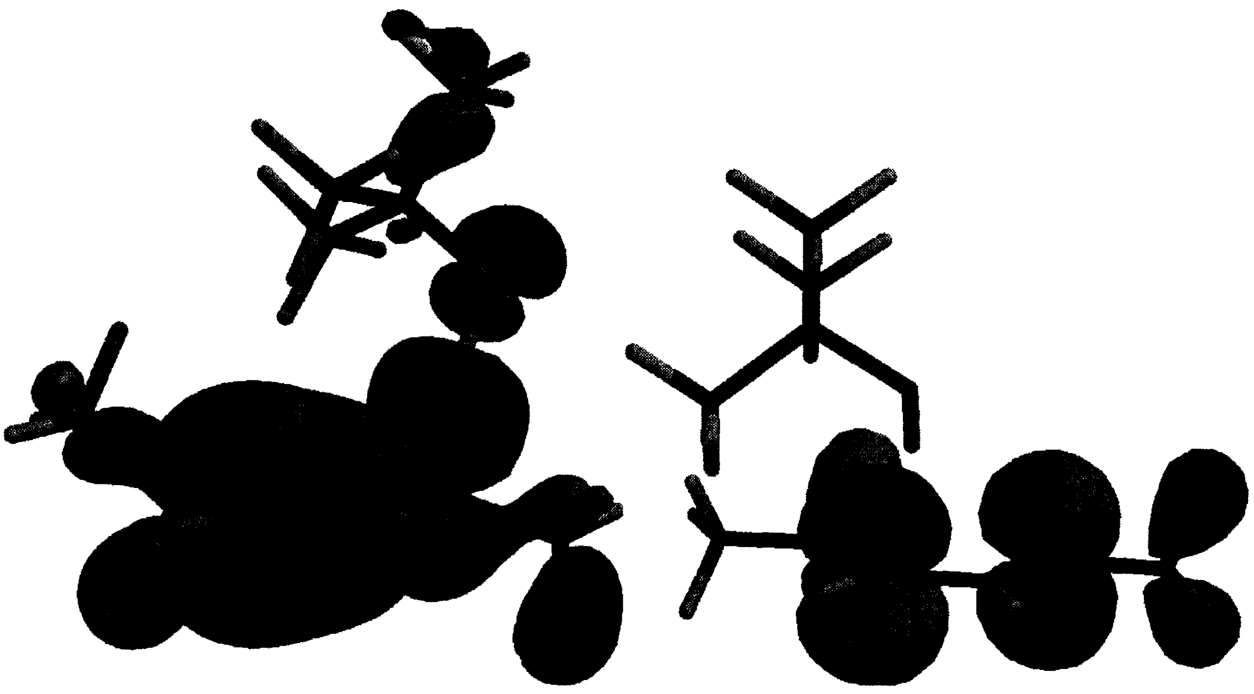
In all the four model cases studied, the values obtained for the imaginary vibrational frequency which represents the reaction coordinate (table 2) were considerable ($|\nu| > 1000$ cm^{-1}). This indicates a "peaky" TS, with a well-defined geometry for the activated complex.[17, 18] A rough estimate of the location of the TS along the reaction coordinate can be obtained by comparing (Fig. 1) the HOMO of the TS with that of the reaction products. Thus, an early, reactant-like TS would show double bond character, while a late, product-like TS would evidence allylic hybridization.



(a) (b)

Fig. 1. Expected HOMO for (a) an early TS; (b) a late TS.

Such a comparison shows that allylic hybridization does not form in the HOMO of the TS, but only in the products. An example, depicting HA from the model substrate 3-hexene, is shown in Fig. 2. Similar MO configurations were obtained for cyclohexene, cyclopentene, and 2-pentene. Indeed, an early TS is in accordance with the Hammond principle[19] in this case, as all four reactions are exothermic.

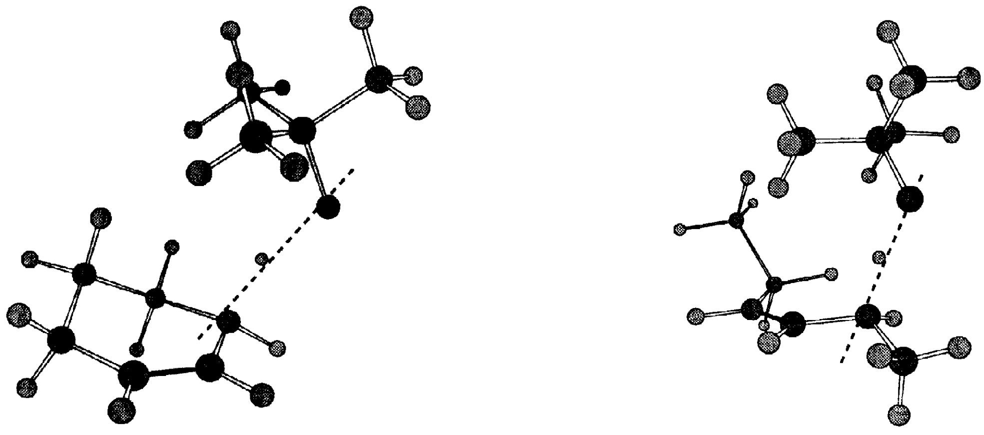


(a) *(b)*

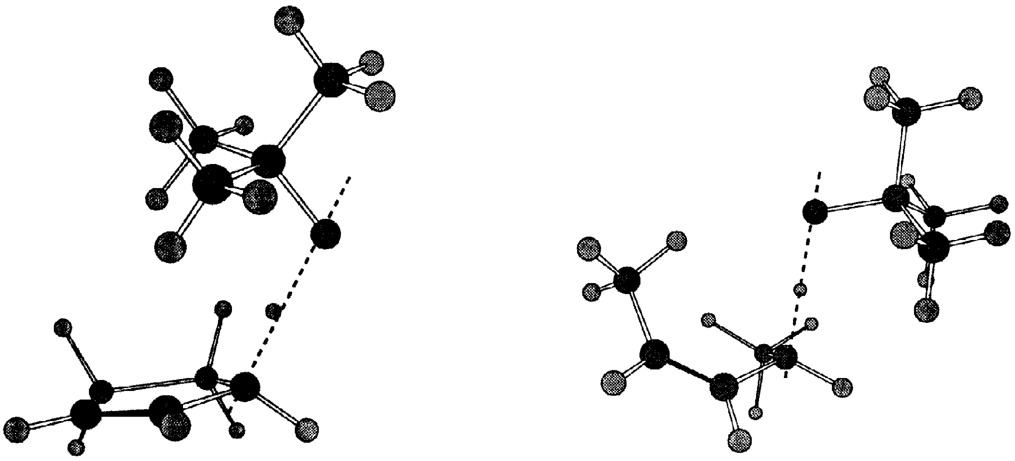
Fig. 2 Computed HOMO for *(a)* TS; *(b)* products of HA from 3-hexene.

Another question worthy of discussion is the linear alignment of the C-H-O atoms in the TS (Fig. 3, the linearity is emphasized by dashed lines). The dissociation energies for benzylic and 1^0 allylic C-H bonds are reported to be the same (ΔH^0_d=85±1 kcal/mol), with equal resonance energies (19±2 kcal/mol relative to the methyl radical).[20, 21] However, the 1^0 allylic position can be up to twice as reactive as the benzylic position towards HA.[5] A possible explanation for this reactivity difference can be found in the work of Kwart *et al*, who suggested that allylic double bonds form a cyclic activated complex with alkoxy radicals, whereas phenyl groups do not. Kwart's elegant kinetic isotope effect (KIE) experiments showed that the KIE for allylic HA with *tert*-butoxy radicals was higher than the predicted maximum for a linear TS.[22, 23]

Our calculations, however, indicate that for all four model substrates, the activated complex should be linear or almost linear. Furthermore, MO representations do not evidence overlapping of the oxygen p-orbitals and the double-bond π-orbital.[24]



Cyclohexene 3-Hexene



Cyclopentene 2-Pentene

Fig. 3. Optimized Transition State Geometries.

CONCLUSION

The entropy of activation does not appear to be a primary factor in the cyclic activation of allylic hydrogens. Explanation of this effect in terms of E_a and $\Delta H^{\ddagger}$ seems more appropriate. Ring strain, bond strengths, and resonance energies would be important in this approach, in agreement with Ingold's suggestions.[13]

PROGRAMS AND METHODS

All calculations were carried out at the semiempirical Unrestricted Hartree-Fock (UHF) AM1 level, using SPARTAN™ version 4.1[25] and AMPAC™ version 5.0.[26] Starting geometries of transition structures were taken from the results obtained by the linear synchronous transit method.[27] Harmonic frequencies were computed for stationary structures. Energy minimum structures had all real frequencies, and transition structures had only one imaginary frequency, associated with the negative force constant for motion along the reaction coordinate.

Acknowledgments
Computer facilities were kindly provided by Prof. David Avnir of the Chemistry Institute of the Hebrew University of Jerusalem. Instructive discussions, on computational methods and their implementation, with Dr. David Danovitch, Dr. Nathan Harris, Yariv Pinto and Shahar Keinan are greatfully acknowledged.

REFERENCES AND NOTES

1. Sheldon, R. A.; Kochi, J. K. *Metal-catalyzed Oxidations of Organic Compounds;* Academic: New York, 84, 1981; pp. 25-26.
2. Szmant, H. H., *Organic Building Blocks of the Chemical Industry,* Wiley: New York, 1989; pp. 386-391.
3. Bridgehead allylic positions are the exception to this rule. See Busfield, W. K.; Grice, I. D.; Jenkins, I. D., *Aust. J. Chem.,* **1991**, 44, 1407-1415.
4. Walling, C.; Rieger, A. L.; Tanner, D. D., *J. Am. Chem. Soc.*, **1963**, 85, 3129-3134.
5. Bridger, R. F.; Russell, G. A., *J. Am. Chem. Soc.*, **1963**, 85, 3754-3765.
6. Howard, J. A.; Ingold, K. U., *Can. J. Chem.,* **1967**, 45, 793-802.
7. Walling, C.; Thaler, W., *J. Am. Chem. Soc.,* **1961**, 83, 3877-3884.
8. Russell, G. A.; De Boer, C., *J. Am. Chem. Soc.*, **1963**, 85, 3136.
9. Courtneidge, J. L.; Bush, M., *J. Chem. Soc. Perkin Trans. 1.*, **1992**, 1531-1538.
10. Bernardi, R.; Caronna, T.; Coggiola, D.; Ganazzoli, F.; Morrocchi, S., *J. Org. Chem.*, **1986**, 51, 1045-1050.
11. Kooyman, E. C., *Disc. Faraday Soc.,* **1951**, 10, 163-174.
12. Courtneidge, J. L.; Bush, M., *J. Chem. Soc. Chem. Commun.,* **1989**, 1227-1229.
13. Ingold, K. U., *Intern. Symp. Free Radical Soln.,* Univ. of Michigan, Ann Arbor, Mich., **1966**, 49-67.
14. Rothenberg, G.; Yatziv, Y.; Sasson, Y., *Tetrahedron,* **1998**, 54, 593-598.
15. Moore, W. J., *Physical Chemistry;* 4th ed., Prentice-Hall: New York, **1972**, pp. 385-387.
16. Values were calculated per active hydrogen atom. In the cyclic molecules it was assumed that both allylic hydrogens have equal reactivity, although preferential HA from the pseudo-axial positions of

six-membered rings has been suggested. See, for example, Beckwith, A. L. J.; Phillipou, G., *Aust. J. Chem.*, **1976**, 29, 1277-1294; Cross, B.; Whitham, G. H., *J. Chem. Soc.*, **1961**, 1650-1654.

17. Busfield, W. K.; Grice, I. D.; Jenkins, I. D.; Monteiro, M. J., *J. Chem. Soc. Perkin Trans. 2.*, **1994**, 1071-1077.
18. Evans, M. G.; Polanyi, M., *Trans. Faraday Soc.*, **1938**, 34, 11-29.
19. Hammond, G. S., *J. Am. Chem. Soc.*, **1955**, 77, 334-338.
20. Huyser, E. S., *Free-Radical Chain Reactions;* Wiley-Interscience: New York, 1970, pp. 68-69.
21. Reactivity comparisons based on bond strengths alone are somewhat problematic, as ΔH^{0}_{d} values vary depending on the technique of measurement. See, for example, Golden, D. M.; Benson, S. W., *Chem. Rev.*, **1969**, 69, 125, where $\Delta H^{0}_{d,\ \text{allylic C-H}}=89\pm1$ kcal/mol. Based solely on bond strengths, this value would support a lower reactivity for 1^{0} allylic hydrogens, relative to benzylic ones, whereas the opposite has been observed experimentally. In another example, $\Delta H^{0}_{d}=80\pm1$ kcal/mol for pentadien-1,4-yl-3, while for the more reactive cyclopentadien-1,3-yl-5 $\Delta H^{0}_{d}=81.2\pm1.2$ kcal/mol.[28]
22. Kwart, H.; Benko, D. A.; Bromberg, M. E., *J. Am. Chem. Soc.*, **1978**, 100, 7093-7094.
23. Kwart, H., *Acc. Chem. Res.*, **1982**, 15, 401-408.
24. It should be noted, however, that our computations pertain to the gas phase, while Kwart's experiments were performed in solution.
25. SPARTAN version 4.1, Wavefunction Inc., 18401 Von Karman Ave., #370, Irvine, CA 92715 U.S.A. © 1995 Wavefunction Inc.
26. AMPAC version 5.0, 1995 Semichem, 12715 W. 66th Terrace, Shawnee, KS 66216, U.S.A.
27. LST method as implemented in the SPARTAN program. See also Halgren, T. A.; Lipscomb, W. N., *Chem. Phys. Lett.*, **1977**, 49, 225-232.
28. Furuyama, S.; Golden, D. M.; Benson, S. W., *Int. J. Chem. Kinet.*, **1971**, 3, 237.