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A FORCE-FIELD STUDY OF ALKENYL RADICAL RING CLOSURE

Athelstan L.J. Beckwith* and Carl H. Schiesser

Research School of Chemistry, Australian National University, Canberra, Australia, 2601.

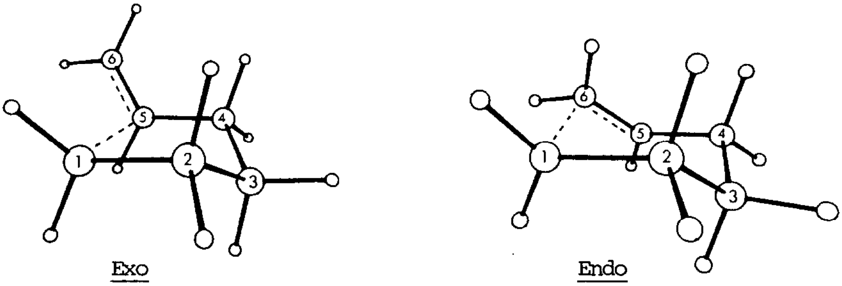
Summary: In accord with stereoelectronic considerations there is a good correlation between the relative rates, regiochemistry, and stereochemistry of ring closure of ω-alkenyl radicals, and the strain energies of transition structures determined by force field calculations.

Theoretical studies[1] of the ring closure of ω-alkenyl radicals have met with only limited success. Thus, MINDO/3 calculations[1] give activation energies considerably larger than those obtained experimentally[2] and fail to predict the observed degree of preference for exo-cyclisation of 5-hexenyl and 6-heptenyl radicals.

Since the qualitative rationalisation of the preferential exo-cyclisation of suitably constituted alkenyl radicals rests on stereoelectronic considerations[3] the use of a theoretical method specifically designed to evaluate strain energies appears appropriate. We have therefore used Allinger's MM2 program[4] to test the validity of the assumption for 5-hexenyl radical cyclisation "that the strain engendered in accommodating the mandatory disposition of reactive centres within the transition complex for 1,6-ring closure outweighs those steric and thermochemical factors expected to favour the formation of the more stable possible product".[3]

Initially, we used models for the transition structures for exo and endo ring closure of hexenyl radical incorporating dimensions for the C1,C5,C6 array (the "intimate" transition structure) obtained from ab-initio studies of methyl radical addition to ethylene.[5] However, the difference in strain energy between the exo transition structure and the endo structure obtained by the MM2 method was considerably larger than the difference between the corresponding experimental activation energies.[2] We attribute this outcome to the fact that the actual dimensions of the C1,C5,C6 array will reflect the interplay of steric and electronic energies and will not, therefore, be the same in the exo structure as in the endo. Accordingly, calculations by the MNDO-UHF[6] method were carried out on the hexenyl system to obtain the following dimensions for the two transition structures:- exo: C1-C5, 2.20 Å; C5-C6, 1.388 Å; C1C5C6, 104°; endo: C1-C6, 2.20 Å, C5-C6, 1.392 Å, C1C6C5, 98°.

Transition structures for cyclisation of 5-hexenyl radical incorporating these fixed dimensions were then treated by the MM2 method to obtain the strain energies of their most stable comformers (see figure). Subtraction in each case of the ground state strain energy of the radical and of the steric energies associated with the close approach of C1 and C5 (or C1 and C6) and with the stretching of the C5–C6 bond gave values of ΔE_s, the strain energy associated with formation of the model *exo* and *endo* transition structures from hexenyl radical. As expected on stereoelectronic grounds[3] the calculated value of ΔE_s for the *exo* transition structure is less than that for the *endo*. The difference between them (2.8 kcal.mol^{-1}) is somewhat larger than that observed experimentally (1.7 kcal.mol^{-1}) but this is reasonable since our calculations make no allowance for the more favourable electronic energy change associated with formation of the *endo* structure.



Exo

Endo

Figure. Model transition structures for cyclisation of 5-hexenyl radical

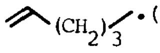
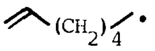
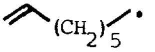
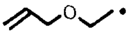
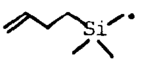
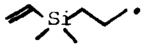
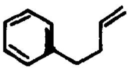
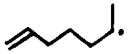
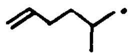
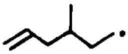
Other radicals were treated similarly (see Table). In most cases a special radical force-field[7] was used for C1, but in some (**8**-**10**), C1 was regarded as sp^2 carbon. The dimensions of the C1C5C6 array specified above were used as appropriate in every case except for the alkynyl radical (**7**) for which the C5–C6 distance was set at 1.2 A in both *exo* and *endo*.

Scrutiny of the data in the Table reveals the following noteworthy features.

(i) *Regiochemistry*. For each of the radicals except (**3**) the calculations correctly predict the regiochemistry of ring closure. This is especially significant in the case of **4** and **8**, two of a relatively small number of radicals known to undergo preferential *endo* ring closure.[3] Furthermore, the difference between calculated values of ΔE_s(*endo*) and ΔE_s(*exo*) gives a rough indication of the relative yields of cyclic products. This concordance between theory and experiment lends further credence to the stereoelectronic approach to radical cyclisation.[3] The failure of octenyl radical (**3**) to conform to this otherwise general pattern suggests that further scrutiny of this system is justified.

(ii) *Stereochemistry*. There is remarkable agreement between theory and experiment for ring closure of the monosubstituted hexenyl radicals (**11**)-(**14**), for each of which the calculations correctly predict the predominant stereo-isomer. In the case of the radicals (**12**-**14**) the difference in strain energies clearly reflects the conformational preference of the substituent in the cyclohexane-like *exo* transition structure[3] (see figure). The calculated preference for formation of the *cis* product from the radical (**11**) substituted at C1 was, however, not expected. Detailed examination of the strain energy components reveals that the non-bonded interaction between the methyl substituent and C6 in the *cis* transition structure is less important than that between the methyl and the proton on C5 in the *trans*.

Table. Transition Structure Strain Energies^a and Experimental Kinetic Data^a for Ring Closure of ω-Alkenyl and Related Radicals

Radical	E_s(ground)	ΔE_s(exo)	ΔE_s(endo)	k_{25}(exo)	k_{25}(endo)	E_{act}(exo)	E_{act}(endo)	Ref
 (1)	2.9	7.5	10.3	2.3x10^5	4.1x10^3	6.8	8.5	2
 (2)	3.5	9.2	10.5	5.2x10^3	8.3x10^2	7.9	8.8	2
 (3)	4.2	15.8	15.3	1.2x10^2	<7x10^1	9.6	na	2
 (4)	3.4	9.7	9.5	6.1x10^3	9.0x10^3	8.5	7.9	8
 (5)	6.5	6.1	9.2	5.2x10^6	<1x10^5	5.1	na	9
 (6)	6.0	5.2	11.1	8.5x10^6	<1x10^5	4.1	na	10
 (7)	2.3	7.5	14.7	2.8x10^4	<6x10^2	8.3	na	10
 (8)	-0.4	9.8	6.7	8.7x10^2	1.8x10^3	na	na	11
 (9)	-0.3	7.4	9.7	7.4x10^4	5.0x10^3	na	na	11
 (10)	0.80	5.6	9.9	3.1x10^8	<6x10^6	3.7	na	10
		ΔE_s(cis)	ΔE_s(trans)	k_{25}(cis)	k_{25}(trans)	E_{act}(cis)	E_{act}(trans)	
 (11)	3.4	7.4	7.5	1.1x10^5	4.2x10^4	6.9	7.6	8
 (12)	4.7	7.3	6.3	2.4x10^5	4.5x10^5	6.5	6.1	9
 (13)	4.5	6.1	7.7	7.0x10^5	2.4x10^5	6.0	6.4	9
 (14)	5.0	7.9	6.2	7.5x10^4	3.6x10^5	7.7	6.6	9

[a] Energies in kcal.mol^{-1}, rate constants at 25° in s^{-1}; na: not available.

(iii) *Relative rates*. Within any group of closely related radicals there is remarkable agreement between the predicted order of reactivity and the experimental rate constants. Thus for the radicals (1-7) the predicted order of reactivity for *exo* ring closure, *viz.* 6 > 5 > 1 = 7 > 2 > 4 > 3 is almost the same as that observed experimentally, and the only major difference (between 4 and 2) can be reasonably ascribed to entropic factors. Similarly, for the radicals (11-14) the predicted order of reactivity, 13c > 14t > 12t > 12c > 11c > 11t > 13t > 14c, is very similar to the experimental: 13c > 12t > 14t > 12c = 13t > 11c > 14c > 11t. Not surprisingly, considering the crudeness of the model and the probable experimental errors, the agreement between values of ΔE_s and activation energies is less impressive. Nevertheless it is noteworthy that for *exo* cyclisation of the majority of radicals in the table, E_{act}(*exo*) lies within 1 kcal.mol^{-1} of ΔE_s(*exo*).

Extension of this investigation has shown that force-field calculations provide reliable predictions of the behaviour of more complex systems. These together with further examples of simple alkenyl analogs will be discussed in the full paper.

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References and Notes

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