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AM1 AND POLARIZED-π FRONTIER MOLECULAR ORBITAL (PPFMO) STUDIES OF FACIAL SELECTIVITY IN HYDROGEN TRANSFER TO SUBSTITUTED ADAMANTYL RADICALS

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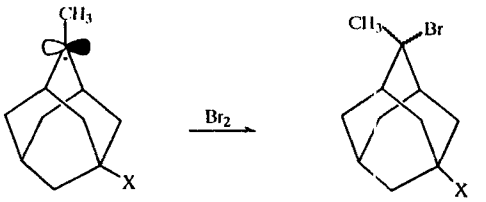
Fully optimized transition states for hydrogen transfer from methane and propene to substituted 2-adamantyl radicals were calculated using the AM1 molecular orbital method. Methane and propene were chosen to provide an early (propene) and a late (methane) transition state. For 5-substituted radicals (F, Cl, Ph, CH_3, CF_3) the enthalpic differences between *syn* and *anti* reactions was found to be small [$<0{\cdot}1$ kcal mol^{-1} (1 kcal = 4·184 kJ)]. Other radicals with nitrogen or boron included directly in the adamantyl fragment showed greater selectivities, with aza substitution favoring *syn* and bora substitution favouring *anti* attack, as did the 4,9-difluoro derivative. The calculated selectivities are all in qualitative agreement with experimental results (where available) on bromine atom transfer. PPFMO calculations showed the polarization of the SOMO to be generally in accord with the AM1 results, whereas the polarization of the LUMO's was less indicative. The bond orders for the bonds *syn* and *anti* to the incipient C—H bond in the adamantyl fragments indicated that the *anti* bonds were always weaker than those *syn*, in agreement with the suggestion by Cieplak that has been used to explain the experimental selectivities. However, the bond lengths of the incipient C—H bonds are always shorter for the side of preferred attack, in apparent agreement with the suggestion by Anh.

INTRODUCTION

Electronic control of facial selectivity has been the subject of significant recent interest. Le Noble and co-workers[1–6] have reported many of the most interesting experimental results, generally using substituents on the 5-position of adamantanone and other adamantane derivatives to provide electronic influences with negligible steric effects on the selectivity. They generally interpreted their results as agreeing with the suggestions previously made by Cieplak.[7] We have shown that the facial selectivities of the reductions of carbonyl groups, including all the adamantanone derivatives, could be explained[8] using the recently formulated polarized-π frontier molecular orbital theory (PPFMO).[9]

The Cieplak argument[7] suggests that the dominant electronic interaction should be the interaction of the σ* orbital of the incipient bond with an antiperiplanar bond on an adjacent position. The argument requires both that the incipient σ-bond be polar and the transition state be early. In such a situation, the σ* orbital resembles the LUMO of the π-system. Hence the Cieplak suggestion should work for early (rather than late) transition states. PPFMO, like all FMO formulations, should also work best for early transition states. In a recent analysis of several models for diastereoselectivity, Li and Le Noble[10] came to a similar conclusion using a different approach.

Bodepudi and Le Noble[11] reported that the radical hydrobromination of methyleneadamantanes occurs with facial selectivities similar to those for the reductions of the analogous ketones. The product-determining step in this reaction is the transfer of a bromine atom from Br_2 to a methyladamantyl radical [reaction (1)]. This result is surprising because the tran-



Reaction 1

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sition state should not be as early nor the incipient bond as polar as in carbonyl reductions. In the hope of clarifying the situation, we report here a detailed study of the transition states for radical abstractions by 5-substituted adamantyl and other related radicals.

METHODS

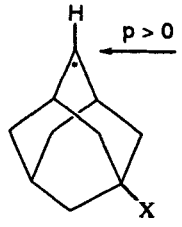
The transfer of a hydrogen atom between adamantyl radicals and another alkyl radical was chosen as a model reaction for two reasons. We encountered calculational difficulties in attempts to optimize reactions involving bromine atom transfer. Previous reports of AM1 calculations on H-transfer reactions between carbon-centered radicals,[12,13] and other AM1 studies on free radical reactions,[14-16] have agreed well with experimental results. For the latter reason, we chose the AM1 molecular orbital method[17] for the optimization of the transition states. In order to evaluate the effect of the earliness of the transition state, both methyl and allyl were used as the other alkyl radical. If one takes the reaction direction as transfer from the alkyl radical to the adamantyl radical, the transfer from allyl will be early (exothermic), whereas that from methyl will be late (endothermic).

The transition states were completely optimized in all internal coordinates using the AMPAC 2.1 program on IBM RS/6000 workstations. The force constants for each optimized transition state were calculated to verify the correct number (1) of negative force constants in each case. The half electron method[18] was used as it is known to give better radical energies and has been successful in several other AM1 studies of free radical reactions.

The PPFMO calculations were performed on AM1-optimized geometries using the STO–3G basis set with additional s-functions only on the p-orbital containing the unpaired electron. The RS/6000 version of the GAUSSIAN 92[19] program was used for this purpose. The distances from the nucleus and exponents were kept at the values used previously.[9]

RESULTS AND DISCUSSION

Tables 1 and 2 present the $\Delta H_{formation}$ values for the optimized transition states for the abstraction from methane and propene, respectively. Since the differences in the energies of the diastereomeric transition states are so small, the $\Delta H_{formation}$ values rather than $\Delta H^{\ddagger}$ values are reported to minimize rounding errors. As can be seen from Tables 1 and 2, the differences in the $\Delta H_{formation}$ values are very small [$>0{\cdot}1$ kcal mol^{-1} (1 kcal = 4·184 kJ)] for the 5-substituted adamantyl radicals **Ia–e**. In all cases, the differences are greater for



I

a: X=F
b: X=Cl
c: X=ph
d: X=CH_3
e: X=CF_3

Table 1. AM1-optimized transition states for abstraction from methane (energies in kcal mol^{-1}, distances in Å)

Compound	ΔH_f (TS) *syn*	ΔH_f (TS) *anti*	$\Delta\Delta H^{\ddagger}$	Attack	C—H—C_{ad} *syn*	C—H—C_{ad} *anti*
Parent	2·713	2·713	0		1·344–1·267	1·334–1·267
Ia	−40·318	−40·329	0·011	*anti*	1·341–1·269	1·342–1·267
Ib	−2·898	−2·828	−0·070	*syn*	1·343–1·267	1·343–1·267
Ic	35·334	35·341	−0·007	*syn*	1·344–1·267	1·344–1·266
Id	−0·975	−0·980	0·005	*anti*	1·345–1·267	1·345–1·267
Ie	−153·186	−153·135	−0·051	*syn*	1·341–1·269	1·339–1·272
II	49·184	49·343	−0·159	*syn*	1·339–1·270	1·337–1·271
III	30·318	30·175	0·143	*anti*	1·344–1·264	1·345–1·264
IV	−17·299	−17·568	0·269	*anti*	1·352–1·259	1·352–1·259
Va	98·519	99·485	−0·966	*syn*	1·338–1·268	1·318–1·283
Vb	98·102	98·581	−0·479	*syn*	1·329–1·273	1·320–1·282
Vc	102·612	102·61	0·002	*anti*	1·319–1·282	1·321–1·280
VIa	40·705	41·517	−0·812	*syn*	1·339–1·266	1·321–1·280
VIb	40·612	40·900	−0·288	*syn*	1·331–1·272	1·324–1·278
VIc	44·457	44·147	0·310	*anti*	1·321–1·281	1·322–1·280
VII	−86·557	−86·211	−0·346	*syn*	1·342–1·269	1·337–1·272

Table 2 AM1-optimized transition states for abstraction from propene (energies in kcal mol^{-1}, distances in Å)

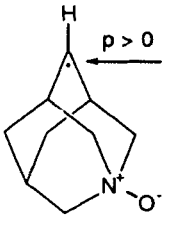
Compound	ΔH_f (TS) *syn*	ΔH_f (TS) *anti*	$\Delta\Delta H^{\ddagger}$	Attack	C—H—C$_{ad}$ *syn*	C—H—C$_{ad}$ *anti*
Parent	16·631	16·631	0		1·309–1·332	1·309–1·332
Ia	−26·377	−26·311	−0·066	*syn*	1·306–1·333	1·305–1·335
Ib	11·047	10·999	0·048	*anti*	1·304–1·335	1·304–1·334
Ic	49·157	49·191	−0·034	*syn*	1·308–1·333	1·309–1·332
Id	12·963	12·950	0·013	*anti*	1·309–1·330	1·308–1·332
Ie	−139·212	−139·117	−0·095	*syn*	1·304–1·336	1·304–1·336
II	63·085	63·288	−0·203	*syn*	1·303–1·337	1·301–1·337
III	44·080	44·000	0·080	*anti*	1·306–1·333	1·307–1·332
IV	−3·533	−4·014	0·481	*anti*	1·318–1·324	1·316–1·326
Va	112·458	113·602	−1·144	*syn*	1·300–1·336	1·286–1·350
Vb	112·099	112·745	−0·646	*syn*	1·291–1·344	1·286–1·348
Vc	116·554	116·915	−0·361	*syn*	1·283–1·351	1·286–1·348
VIa	54·652	55·888	−1·236	*syn*	1·302–1·334	1·290–1·346
VIb	54·616	55·329	−0·713	*syn*	1·292–1·342	1·291–1·345
VIc	59·291	58·679	0·612	*anti*	1·286–1·348	1·291–1·345
VII	−72·570	−72·218	−0·352	*syn*	1·305–1·336	1·303–1·338

the earlier transition state (abstraction from propene). It is inadvisable to interpret energy differences of less than 0·1 kcal mol^{-1}, but one should note that there is qualitative agreement with the experimental report and the general trend is what might be expected from the selectivities of the adamantanone reductions. Nevertheless, the selectivities calculated from these energy differences at 298 K are all >0·1 kcal mol^{-1}, and therefore negligible.

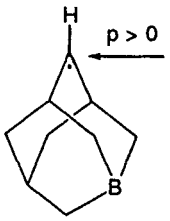
The differences in the ΔH_f values of the transition states are larger for the radicals with a nitrogen or boron in the skeleton, **II**–**IV**. The calculations suggest that radical **II** be preferentially attacked from the *syn* side. The bora-radical **III**, and especially its ammonium salt **IV**, should have the opposite (*anti*) selectivity. No experimental results have been reported for similar cases.

The di- and triazaadamantyl radicals **Va–c** and **VIa–c** are complicated by the possibility that each of the N—H bonds can assume two conformations, leading to a total of three for each case. The predicted selectivities are dependent on the conformations, as seen from the tables. Experimental results on similar radicals would be difficult to interpret as one could not know the conformation operative in the transition state. For this reason, we studied the difluoro-radical **VII**, which has a selectivity similar to those of **Va** and **VIa**.

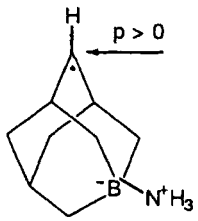
According to the suggestion made by Cieplak and applied to adamantyl systems by Le Noble and coworkers, the stabilization of the transition state for the favored attack should come from the interaction of the antibonding orbital associated with the incipient bond with the bonding orbitals of the antiperiplanar σ-bonds on the carbons adjacent to the site of attack. The result of this interaction should be to weaken the bonds *anti* to the attack relative to the corresponding bonds *syn* to the attack. A similar result would be expected from the Anh analysis,[20] as charge would be transferred to the σ^* orbitals of the bonds *anti* to the attack. To test this, we examined the bond orders of the σ-bonds involving these carbons in the optimized transition states. We selected transition states for the reactions (both *syn* and *anti*) of **Ia** and **III** with both methane and propene,



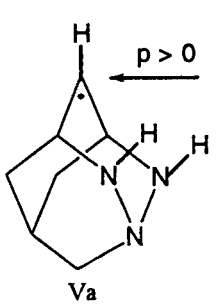
II



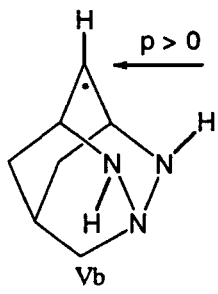
III



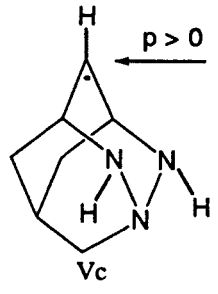
IV



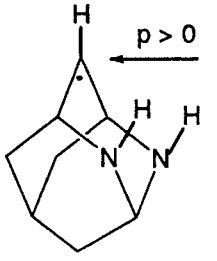
Va



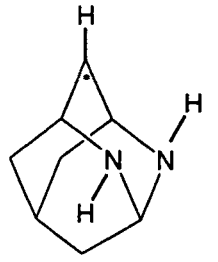
Vb



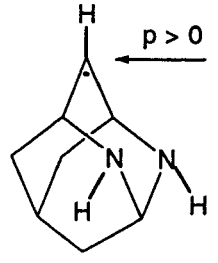
Vc



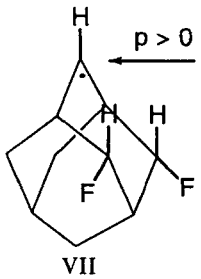
VIa



VIb



VIc



VII

since **Ia** shows a low and **III** a high (calculated) selectivity and methane and propane allow us to examine early and late transition states. The bond orders *anti* were always weaker than those corresponding to the equivalent bonds on the side *syn* to the site of attack. The qualitative results were always the same whether the attack was *syn* or *anti* to the substitution.

Hence the results are in agreement with Cieplak's and Anh's suggestions (both of which were originally made for the reduction of carbonyls, not radical reactions). Li and Le Noble[10] have shown that Cieplak's suggestion seems more valid for early and Anh's for late transition states. We have also pointed out[8] that Cieplak's formulation extrapolates to an FMO argument for early transition states, whereas Anh's extrapolates to a similar FMO argument for late transition states. Cieplak applied his argument to nucleophilic attacks where the transition state is early and the incipient bond highly polarized.[7] The observation that the optimized transition states have characteristics consistent with both Anh's and Cieplak's suggestions agrees with both Le Noble and co-workers' and our own analyses. As the free radical atom transfer reactions do not have particularly early transition states, one might expect them to exhibit the characteristics of both interactions.

Tables 3 and 4 present the PPFMO results for the SOMOs and LUMOs of the radicals. The polarizations are negligible for the SOMOs ($<0{\cdot}005$) and small for the LUMOs ($<0{\cdot}025$) of all of the 5-substituted radicals **Ia–e**, in general agreement with the AM1 transition-state energies. The SOMO polarizations are all in the same direction as the AM1 selectivities except for that of **Id**, where AM1 predicts 0·005 and 0·013 kcal mol^{-1} selectivities for the *anti* attacks in the two abstraction reactions, whereas PPFMO predicts *syn* attack. The LUMO selectivities are the same as those for the SOMO except that **Ic** favors *anti* attack (in disagreement with both the SOMO and the AM1 trasition sites). For compounds **II**, **III**, **IV** and **VII**, the SOMO agree with the AM1 transition states. The polarizations of the LUMOs are all in the same direction except for that of **III**.

We have previously suggested that the SOMO polarizations should be more important than those of the LUMO for atom-transfer reactions.[9] The present results seem to support this view. The Cieplak argument might imply that the LUMO is more important as the interaction of this orbital with its corresponding spin orbital of the C—H bond will be more polarized as the electron is originally on the methane or propene.

Table 3. PPFMO results for the SOMOs

Compound	Coefficient on s-function		p	Coefficient on p-orbital	E^{SOMO}	Predicted attack	$-p/E^{SOMO}$
	syn	*anti*					
Ia	0·24236	−0·24235	0·00001	0·75271	−0·2824	*syn*	0·0000
Ib	0·23919	−0·24018	−0·00099	0·74573	−0·288	*anti*	−0·0034
Ic	0·24507	−0·24436	0·00071	0·73916	−0·2732	*syn*	0·0026
Id	0·2452	−0·24437	0·00083	0·73955	−0·2708	*syn*	0·0031
Ie	0·24316	−0·23818	0·00498	0·7383	−0·2842	*syn*	0·0175
II	0·2381	−0·2365	0·0016	0·7449	−0·2999	*syn*	0·0053
III	0·23424	−0·24533	−0·01109	0·76103	−0·2788	*anti*	−0·0398
IV	0·24528	−0·26175	−0·01647	0·74386	−0·2379	*anti*	−0·0692
Va	0·15452	−0·16704	−0·01252	0·5029	−0·2667	*anti*	−0·0469
Vb	0·0371	−0·13701	−0·09991	0·55904	−0·3134	*anti*	−0·3188
Vc	0·07829	−0·20297	−0·12468	0·73682	−0·3107	*anti*	−0·4013
VIa	0·21202	−0·2165	−0·00448	0·72702	−0·2849	*anti*	−0·0157
VIb	0·20752	−0·21058	−0·00306	0·6592	−0·2805	*anti*	−0·0109
VIc	0·05432	−0·20169	−0·14737	0·70527	−0·3009	*anti*	−0·4898
VII	0·25872	−0·22276	0·03596	0·7124	−0·2852	*syn*	0·1261

Table 4. PPFMO results for the LUMOs

Compound	Coefficient on s-function		p	Coefficient on p-orbital	E^{LUMO}	Predicted attack	p/E^{LUMO}
	syn	*anti*					
Ia	0·67937	−0·67465	0·00472	0·44761	0·17053	*syn*	0·0277
Ib	0·66944	−0·68071	−0·01127	0·44972	0·16423	*anti*	−0·0686
Ic	0·67666	−0·68351	−0·00685	0·44401	0·17554	*anti*	−0·0390
Id	0·68814	0·67457	0·01357	0·44404	0·17843	*syn*	0·0761
Ie	0·68829	−0·66512	0·02317	0·44793	0·1668	*syn*	0·1389
II	0·66303	−0·67883	−0·0158	0·45298	0·15414	*anti*	0·1025
III	0·63362	−0·69475	−0·06113	0·44769	0·17408	*anti*	−0·3512
IV	0·65263	−0·72598	−0·07335	0·4324	0·20823	*anti*	−0·3523
Va	0·7393	−0·57315	0·16615	0·43342	0·15304	*syn*	1·0857
Vb	0·65352	−0·65079	0·00273	0·45596	0·16747	*syn*	0·0163
Vc	0·55769	−0·72533	−0·16764	0·47342	0·17762	*anti*	−0·9438
VIa	0·73184	−0·59232	0·13952	0·43352	0·16118	*syn*	0·8656
VIb	0·65397	−0·65655	−0·00258	0·45442	0·1742	*anti*	−0·0148
VIc	0·53726	−0·74123	−0·20397	0·46983	0·18238	*anti*	−1·1184
VII	0·71418	−0·62762	0·08656	0·44873	0·16014	*syn*	0·5405

The calculated selectivities for H-transfer to **Ic**, the compound studied experimentally by Le Noble and coworkers, are lower than the experimental observation (58:42 at 40 °C corresponds to a $\Delta\Delta G^{\ddagger}$ of 0·2 kcal mol^{-1}). The explanation for the difference is difficult to assess with confidence. Among the factors that should be considered are (a) the imperfections of the calculations; (b) the differences between H-transfer and Br-transfer; and (c) the differences between gas-phase (modeled) and solution (experimental) reactions. Clearly, energetic differences of tenths of a kcal mol^{-1} are difficult to model accurately using MO theory. Nevertheless, the calculations do make qualitative predictions for the selectivities of reactions that can be studied in the future. We hope that the selectivities for several of the other compounds that we have studied here will be measured and compared with the present predictions.

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REFERENCES

1. C. K. Cheung, L. T. Tseng, M. H., Lin, S. Srivastava and W. J. le Noble, *J. Am. Chem. Soc.* **108**, 1598 (1986).
2. W. S. Chung, N. J. Turro, S. Srivastava, H. Li and W. J. le Noble, *J. Am. chem. Soc.* **110**, 7882 (1988).
3. M. h. Lin, J. E. Silver and W. J. le Noble, *J. Org. Chem.* **53**, 5155 (1988).
4. H. Li and W. J. le Noble, *Testrahedron Lett.* **31**, 4391 (1990).
5. J. M. Hahn and W. J. le Noble, *J. Am. Chem. Soc.* **114**, 1916 (1991).
6. H. Li, J. E. Silver, W. H. Watson, R. P. Kashyap and W. J. le Noble, *J. Org. Chem.* **56**, 5932 (1991).
7. A. S. Cieplak, *J. Am. Chem. Soc.* **103**, 4540 (1981).
8. X. L. Huang and J. J. Dannenberg, *J. Am. Chem. Soc.* **115**, 6017 (1993).
9. X. L. Huang, J. J. Dannenberg, M. Duran and J. J. Bertran, *J. Am. chem. Soc.* **115**, 4024 (1993).
10. H. Li and W. J. le Noble, *Recl. Trav. Chim. Pays Bas* **111**, 199 (1992).
11. V. R. Bodepudi and W. J. le Noble, *J. Org. Chem.* **56**, 2001 (1991).
12. J. M. Lluch, J. Bertran and J. J. Dannenberg, *Testrahedron* **44**, 7621 (1988).
13. X. L. Huang and J. J. Dannenberg, *J. Org. Chem.* **56**, 5421 (1991).
14. J. J. Dannenberg, in *Advanced Molecular Modeling* edited by D. Liotta, Vol. 2, p. 1. JAE Press, New Haven, CT (1990).
15. D. D. M. Wayner, B. A. Sim and J. J. Dannenberg, *J. Org. Chem.* **56**, 4853 (1991).
16. Huang, X. L. and J. J. Dannenberg, *J. Org. Chem.* **56**, 6467 (1991).
17. M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.* **107**, 3902 (1985).
18. M. J. S. Dewar and J. A. Hashwall, *J. Am. Chem. soc.* **90**, 1953 (1968).
19. *GAUSSIAN 92.* Gaussian, Pittsburgh, PA (1992).
20. N. T. Anh and O. Eisenstein, *Nouv. J. Chim.* **1**, 62 (1977).