Theoretical Study of the Diastereofacial Isomers of Aldrin and Dieldrin

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Abstract: The Diels-Alder reaction of hexachlorocyclopentadiene with norbornadiene gives aldrin but theoretically three other diastereofacial isomers are possible. On oxidation these isomers can generate eight adducts one of which is known as dieldrin. All these, as well as the corresponding reactions with hexafluorocyclopenadiene were studied by semiempirical (AM1 and PM3) and hybrid density functional (B3LYP) methods. Besides the energy levels, the transition states were calculated for the reactions leading to the diastereofacial isomers of aldrin, which indicate that aldrin is the favored product of the reaction both from thermodynamic and kinetic point of view.

Keywords: aldrin, dieldrin, Diels-Alder, semiempirical, density functional

1. Introduction

The Diels-Alder reaction has been extensively applied to both carbodienes and carbodienophiles as well as to heterodienes and heterodienophiles giving rise to a variety of carbocyclic and heterocyclic compounds [1]. We have performed numerous theoretical studies of Diels-Alder reactions by ab initio and density functional methods of this valuable polycyclic reaction [2]. Symmetrical reagents prefer a synchronous concerted pathway where the formation of the two new bonds is taking place at the same time.

An interesting theoretical study of the Diels-Alder reaction of polychlorinated cyclopentadiene to norbornadiene has been recently reported by Marchand et al. [3]. They employed semiempirical AM1 methods to study the transition states and energy levels of this, at one time industrially important reaction. They also applied low level ab initio (HF/3-21) calculations on these AM1 optimized structures to study the transition states of the exo and endo approaches of the diene to the dienophile.

We have undertaken the study of this reaction leading to aldrin and three other diastereofacial isomers using hybrid density functional methods with larger basis sets. The study of the corresponding fluoro derivatives was also investigated in order to compare the effects of these substituents on the reaction pathway. In addition we also studied the semiempirical energy levels of the eight dieldrin stereoisomers which can be obtained from the four aldrin isomers.

2. Results and Discussion

The reaction between hexachlorocyclopentadiene and norbornene gives aldrin, which can be oxidized with peracetic acid to dieldrin, both of which have been used as pesticides (Scheme 1). The systematic name of aldrin is 1,2,3,4,10,10-hexachloro- $1,4,4\alpha,5,8,8\alpha$ -hexahydro-1,4-*exo,endo*-5,8-dimethanonaphtalen, and its structure and numbering are given in Fig. 1.



Scheme 1. The Diels-Alder reaction of hexachlorocyclopentadiene and norbornadiene and oxidation to dieldrin.



Figure 1. 1,2,3,4,10,10-hexachloro-1,4,4 α ,5,8,8 α -hexahydro-1,4-*exo*,*endo*-5,8-dimethanonaphtalen.

Since norbornadiene possesses diastereotopically non-equivalent π -faces two different approaches of the diene to the dienophile are possible. It has been shown experimentally that electrophilic species prefer the exo approach to the norbornadiene C=C double bond [4] but by allowing that an endo approach is also conceivable four isomeric products are possible (Scheme 2).



Scheme 2. Exo and endo approaches of the diene to the dienophile and the four possible diastereofacial products.

The energy levels of the four possible isomers were initially calculated by the AM1 and PM3 semiempirical methods. They are given in Table 1, along with their relative values compared to aldrin (1). Both semiempirical methods predict aldrin to be the most stable isomer, and give comparable values for the energy levels of all four isomers.

The AM1 structures were used as starting points for density functional methods calculations of the reactants, products and transitions states.

The symmetry properties of this addition reaction can be followed by comparing the lengths of the new bonds being formed in the transition states. They are collected in Tables 2 and 3 for the chlorine and the fluorine analogues, respectively. It is immediately apparent that for isomers **1** and **2** of either halogen derivatives the bonds being formed are very similar in lengths leading to the conclusion that the transition states and addition reactions follow a concerted, synchronous mechanism. These are the structures obtained from the endo approach of the diene to the dienophile. The case is different for the exo attack of the dienophile to the diene. In the chloro isomers **3** and **4** the difference in the lengths is 17.5 and 27.6 %, while for the fluoro analogues they are 7.8 and 27.8 %, respectively. The lower value for analogue **3F** is interesting, leading to a possible explanation that there is a strong nodal interaction of the fluorine atom on carbon 10 and the hydrogen atom on carbon 9. The distance between these atoms in the transition state is 1.988 Å which confirms this strong hydrogen bond type of interaction.

	AM1 atmosture	<i>E</i> (AM1)/	$\Delta E(AM1)/$	<i>E</i> (PM3)/	$\Delta E(PM3)/$
	AMT structure	kcal/mol	kcal/mol	kcal/mol	kcal/mol
1	exo endo aldrin	-2587.2	0.0	-2597.5	0.0
2	endo endo	-2584.8	2.4	-2594.5	3.0
3	exo exo	-2576.4	10.8	-2589.4	8.1
4	endo exo	-2575.1	12.1	-2586.5	11.1

Table 1. Relative stabilities of the endo-exo cycloadducts calculated with semiempirical methods.

Table 2. The lengths of the bonds being formed r(a1) and r(a2) in their transition states for the chlorineand fluorine isomers of aldrin calculated at the RB3LYP/6 31++G level.

	C	1	F		
	<i>r</i> (a1)/Å <i>r</i> (a2)/Å		<i>r</i> (a1)/Å	<i>r</i> (a2)/Å	
1	2,359	2,378	2,394	2,397	
2	2,330	2,360	2,374	2,362	
3	2,611	2,153	2,486	2,294	
4	2,840	2,055	2,881	2,080	

Another geometrical feature of these compounds that was compared is the pyramidalization [5] of the halogens bonded to the olephinic carbons at 2 and 3 (angle α) and the hydrogens bonded to the olephinic carbons 4 and 8 (angle β) and 6 and 7 (angle γ). The changes in angle β should be the greatest, for α they should be smaller while angle γ is not directly involved and should experience smaller changes. It was hoped that these distortions from the ideal planar value can be used as a measure for the resistance to product formation: the resistance should be less significant for the

transition state structures whose angle is closer to planar and greater when the deviation from planarity is larger. Except for structures **4**, where the deformations for the two substituents indicate very deformed structures, the results of these comparisons cannot be used to predict the stability of the transition structures and the resistance to their formation. Apparently the dihedral angles are flexible and thus do not reflect accurately the stability of the overall structures.

		Cl		F			
					β(HCCH		
	α(ClCCCl)	β(HCCH)	ү(НССН)	α(CFCCCF))	γ(HCCH)	
1 P	-174.65	119.32	175.05	-169.32	118.98	-175.17	
1 P	-174.66	119.32	175.05	-169.32	118.98	-175.17	
1TS	-175.44	149.43	177.30	-170.31	152.42	-177.49	
1TS	-175.10	149.89	177.26	-170.33	152.32	-177.51	
2P	177.32	115.08	-175.99	-169.92	116.50	-175.91	
2P	177.32	115.08	-175.99	-169.92	116.50	-175.91	
2TS	144.69	147.81	-176.57	-173.25	152.29	-176.63	
2TS	146.48	149.12	-176.55	-173.56	152.55	-176.52	
3P	-174.86	114.88	175.20	-172.38	116.39	175.54	
3P	-174.86	114.91	175.19	-172.39	116.39	175.53	
3TS	-169.28	149.53	177.49	-166.90	142.16	178.30	
3TS	-172.56	132.81	178.30	-167.21	146.31	178.02	
4 P	-174.51	112.33	-174.50	-172.34	114.02	-173.93	
4 P	-174.94	112.31	-174.51	-172.35	114.03	-173.94	
4TS	-168.63	159.90	-173.24	-171.32	134.93	-174.26	
4TS	-173.76	126.29	-174.89	-168.71	159.23	-173.23	

Table 3. Pyrimidalization of the olefin bonds in the products and transition states of the chlorine andfluorine isomers calculated at the RB3LYP/6-31++G level.

Table 4 presents the energy values for the four possible diastereofacial isomers which are also given graphically in Fig. 2. The energies follow the semiempirical calculations showing that isomer **1** is thermodynamically most stable, while isomer **4** is by more than 17 kcal/mol less stable. In Table 4 the energies of the transition states are also presented. The optimized transition state structures are also given in Fig. 3 which can be downloaded as mol files. The pattern is very similar for the transition state energies: the activation energy for **1** is around 24 kcal/mol while for **4** it is by about the same value higher. The calculations performed with polarizations functions on the heavy atoms (B3LYP 6-31+G*) lower the energy by 2-3 kcal/mol but the general pattern is conserved. From these data it can be concluded that with this model chemistry isomer **1** is both thermodynamically and kinetically the favored product of this reaction. To the best of our knowledge we were unable to find in the literature experimental evidence for the presence of isomer **2** although from these calculations it is quite possible that traces of it are formed when obtaining aldrin.

Table 4. Energy levels (ΔE_f), relative energies (ΔE) and transition state energies ($\Delta E^{\#}$) for the aldrin analogues (the value given in bold is with the zero point correction energy).

		Cl		Cl			F			
		B3LYP/6-31++G		B3LYP/6-31+G*			B3LYP/6-31++G			
	Stanoture	$\Delta E_{ m f}$ /	ΔE /	$\Delta E^{\#}$ /	$\Delta E_{ m f}$ /	ΔE /	$\Delta E^{\#}$ /	$\Delta E_{ m f}$ /	ΔE /	$\Delta E^{\#}$ /
	Structure	kcal/mol	kcal/mol	kcal/mol	kcal/mol	kcal/mol	kcal/mol	kcal/mol	kcal/mol	kcal/mol
1 <i>exo endo</i> aldrin		-30.0 -26.1	0.0 0.0	23.9 24.7	-26.9 - 22.8	0.0 0.0	25.9 26.8	-45.4 - 41.2	0.0 0.0	13.0 14.0
2 endo endo		-28.1 - 24.2	1.9 1.9	27.2 27.9	-24.9 - 20.9	1.9 1.9	29.2 30.0	-45.0 - 40.8	0.9 0.7	13.9 14.7
3 exo exo		-14.6 - 10.9	15.4 15.2	36.5 36.9	-12.2 - 8.3	14.7 14.4	37.7 38.5	-37.0 - 32.8	8.9 8.8	21.9 22.8
4 endo exo		-12.6 - 8.9	17.4 17.2	41.17 41.4	-10.5 - 6.6	16.4 16.2	42.7 43.4	-35.0 - 31.0	13.5 12.8	26.5 26.8



Figure 2. Relative energies of the chloro derivatives (1-4) calculated by various methods.



Figure 3. Transition states of the chloro derivatives optimized at the RB3LYP/6-31++G level (available as mol files).

The epoxidation of the double bonds of products 1-4 was studied by semiempirical methods. Since there are two double bonds in these products theoretically the epoxidation can lead to eight different products. The results of the epoxidation of the C-6 C-7 double bond (originating from norbornadiene) is given in Table 5, while the epoxidation of the C-2 C-3 double bond (originating from the hexachlorocyclopentadiene) is given in Table 6. The results are presented graphically in Fig. 4 and 5. From all these results it can be concluded that the epoxidation is thermodynamically preferable at the C-6 C-7 double bond. It is also apparent that the semiempirical methods predict that the most stable isomer is 1a, which is actually the structure of dieldrin.

The two most stable structures 1a and 1b according to the semiempircal methds were optimized at the B3LYP 6-31++G and 6-31+G* levels. Again 1a was more stable, the energy difference being 4,0 and 4,8 kcal, respectively. This only indicates that in the reaction mixture besides dieldrin some other isomers may be present but further calculations with ab initio methods should be undertaken in order obtain more accurate energy values for all isomers.

	AM1 structure	<i>E</i> (AM1) /	Δ <i>E</i> (AM1)/	<i>E</i> (PM3) /	Δ <i>E</i> (PM3)/
		(kcal/mol)	(kcal/mol)	(kcal/mol)	(kcal/mol)
1a		-2667.6	0.0	-2677.7	0.0
1b		-2666.7	0.9	-2675.8	1.8
2a		-2649.7	17.9	-2660.5	17.1
2b		-2663.3	4.3	-2673.2	4.4
3a		-2656.3	11.3	-2668.1	9.6
3b		-2656.9	10.7	-2669.7	7.9
4a		-2653.6	14.0	-2664.3	13.3
4b		-2628.8	38.8	-2645.7	32.0

Table 5. Relative stabilities of dieldrin endo-exo isomers calculated with AM1 and PM3 (epoxidation
of the C-6 C-7 double bond).

	AM1 structure	<i>E</i> (AM1) /	$\Delta E(AM1)/$	<i>E</i> (PM3) /	$\Delta E(PM3)/$
		(kcal/mol)	(kcal/mol)	(kcal/mol)	(kcal/mol)
1c		-2635.3	32.3	-2660.0	17.7
1d		-2642.1	25.5	-2666.6	11.1
2c		-2635.1	32.5	-2655.1	22.6
2d	•	-2636.2	31.4	-2661.1	16.6
3с		-2640.5	27.1	-2661.5	16.1
3d		-2630.8	36.8	-2658.6	19.0
4c		-2639.4	28.2	-2658.6	19.0
4d		-2629.6	38.0	-2655.5	22.2

Table 6. Relative stabilities of dieldrin endo-exo isomers calculated with AM1 and PM3 (epoxidationof the C-2 C-3 double bond).



Figure 4. Relative stabilities of the endo-exo isomers of dieldrin calculated with AM1 and PM3 (epoxidation of the C-6 C-7 double bond).



Figure 5. Relative stabilities of the endo-exo isomers of dieldrin calculated with AM1 and PM3 (epoxidation of the C-2 C-3 double bond).

Computational Methods

All calculations were performed with Gaussian 98 and 03 suites of programs [6,7]. The visualization of the molecules was done with Gauss View [8]. All optimizations were carried out without using any symmetry or other geometry restrictions. Besides the semiempirical AM1 [9] and PM3 [10], the model theory used was restricted Becke's exchange with Lee, Yang and Parr correlation (B3LYP) density functional [11] with the 6-31++G basis set and for some of the structures with polarization functions on heavy atoms with B3LYP/6-31+G*, a model chemistry giving excellent results for energy barrier estimation of pericyclic reactions [12]. Frequency calculations were carried

out with the same basis set for optimization on all structures in order to determine the nature of the stationary points and to obtain zero-point energies. All optimized transition state structures have one and only one imaginary frequency whose motion is along the formation of the new C–C bonds.

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References and Notes

- a) Carruthers, W. Cycloaddition Reactions in Organic Synthesis; Pergamon Press: New York, 1990. b) Brocksom, T. J.; Nakamura, J.; Ferreira, M. L.; Brocksom, U. The Diels-Alder Reaction: an Update. *Journal of the Brazilizan Chemical Society* 2001, *12*(5), 597-622.
- a) Zdravkovski, Z. Theoretical Study of the Diels-Alder Reaction of Benzene with Fluorinated 2. Dienophiles. Journal of Molecular Structture (Theochem) 2004, 684, 99-102. b) Jursic, B. S.; Zdravkovski, Z. Reaction of Imidazoles with Ethylene and Singlet Oxygen. An Ab Initio Theoretical Study. Journal of Organic Chemistry 1995, 60, 2865-2869. c) Jursic, B. S.; Zdravkovski, Z.; Whittenburg, S. L. Ab Initio Study of the Low Reactivity of Thiophene in Diels-Alder Reactions with Carbon Dienophiles. Journal of Physical Organic Chemistry 1995, 8, 753-760. d) Jursic, B. S.; Zdravkovski, Z.; Whittenburg, S. L. Theoretical Study of the Diels-Alder Reaction between S-Methylthiophenium Ion and Ethane. Journal of the Chemical Society, Perkin Transactions 2 1995, 455-459. e) Jursic, B. S.; Zdravkovski, Z. Ab Initio Calculations of Diels-Alder Transition Structures for Heterodienophile Additions to Cyclopentadiene. Journal of Physical Organic Chemistry, 1994, 7, 641-645. f) Jursic, B. S.; Zdravkovski, Z. Ab Initio Study of Heterodienophile Addition to Oxazole. Journal of the Chemical Society, Perkin Transactions 2 1994, 1877-1881. g) Jursic, B. S.; Zdravkovski, Z. Theoretical Study of Ethylene and Vinyl Alcohol Addition to 1,4-Dioxa-1,3-butadiene. Journal of Organic Chemistry 1994, 59, 7732-7736.
- 3. Marchand, A. P; Ganguly, B; Malagón, C. I.; Lai, H; Watson, W. Experimental and Theoretical Studies of Diels-Alder Dimerization of 1,2,3,4,5-Pentachloropentadiene and of Diels-Alder Cycloaddition of Polychlorinated Cyclopentadienes to Norbornadiene. *Tetrahedron* **2003**, 59, 1763-1771.
- a) Mazzocchi, P. H.; Stahly, B.; Dodd, J.; Rondan, N. G.; Domelsmith, L. N.; Rozeboom, M. D.; Carmella, P.; Houk, K. N. π-Facial Stereoselectivity: Rates and Stereoselectivities of Cycloadditions of Hexachlorocyclopentadiene to 7-Substituted Norbornadienes, and Photoelectron Spectral and Molecular Orbital Computational Investigations of Norbornadienes. *Journal of the Americal Chemical Society* 1980, *102*, 6482-6490. b) Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. Origin of π-Facial Stereoselectivity in Additions to π-Bonds: Generality of the Anti-Periplanar Effect. *Journal of the Americal Chemical Society* 1981, *103*, 2438-2440. c) Marchand, A. P.; Chong, H.S.; Ganguly, B.; Coxon, J. M. π-Facial Selectivity in Diels-Alder Cycloadditions. *Croatica Chemica Acta* 2000, *73*, 1027-1038.

- 5. Rondan, N. G; Paddon-Row, M. N.; Caramella, P; Houk, K. N., Nonplanar Alkenes and Carbonyls: A Molecular Distortion Which Parallels Addition Stereoselectivity. *Journal of the Americal Chemical Society* **1981**, *103*, 2436-2438.
- Gaussian 98, Revision A.11.2, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, N. Rega, P. Salvador, J. J. Dannenberg, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, Gaussian, Inc., Pittsburgh PA, 2001.
- Gaussian 03, Revision B.03, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; and Pople, J. A.; Gaussian, Inc., Wallingford CT, 2003.
- 8. Gauss View 03, Gaussian, Inc., Pittsburgh PA, 2003.
- 9. Stewart, J. J. P. Optimization of Parameters for Semi-Empirical Methods I-Method. *Journal of Computational Chemistry* **1989**, *10*, 209-220.
- a) Becke, A. D. A New Mixing of Hartree-Fock and Local Density-functional Theories. *Journal of Chemical Physics* 1993, *98*, 1372-1377. b) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti Correlation Energy Formula into a Functional of the Electron Density. *Physical Review B*, 1988, 37, 785-789.
- Branchadell, V. Density Functional Study of Diels-Alder Reactions Between Cyclopentadiene and Substituted Derivatives of Ethylene. *International Journal of Quantum Chemistry* 1997, *61*(3), 381-388.
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