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Conformational Analysis of Trans-3, 6-Dibutanal-1, 2, 4, 5-Tetroxane

[1]Eduardo A. Castro, [2]Mariela I. Profeta, [2]Jorge M. Romero, [2]Nelly L. Jorge and [2]Manuel E. Gómez Vara
[1]Inifta, Theoretical Chemistry División, Suc.4, C.C. 16, La Plata 1900, Argentina
[2]Facultad de Ciencias Exactas Naturales y Agrimensura, U.N.N.E. Cátedra de Química Física Ic Facena, U.N.N.E., Av. Libertad 5460(3400) Corrientes

Abstract: We report the results of theoretical semiempirical AM1 and PM3 molecular orbital methods on the conformational analysis of the title compound. The relative stability of different isomers and conformers are discussed on the basis of well defined electronic and steric effects, which are rather helpful in order to understand the relative stabilities.

Key words: Conformational analysis, Trans-3, 6-dibutanal-1,2,4,5-tetroxane, Molecular orbital, theory, Semiempirical method-AM1, PM3 calculation techniques

INTRODUCTION

Recently, we have reported some theoretical calculations at the semiempirical level of the isomers of the trans-3,6-dimetoxi-1,2,4,5-tetroxano[1] and other substituted tetroxanes[2,3]. The standard bibliography does not register data on these tetroxane molecules and the improtance of the conformational análisis of tetroxanes with substituents at the axial-axial (trans) location lies on the very fact to verify on them the stereoelectronic effect which make them more stable than the equatorial-equatorial isomers. In fact, this is the form at which they are found in natural compounds which are anti-micotic, anti-malarialc and anti-biotic compounds[4-7].

Nuclear Magnetic Resonance (NMR) and Infrared (IR) spectroscopic studies on some tetroxane derivatives synthesized with ketonic groups, show they adopt a chair conformation and it suggests the most stable isomer is that with substituents at trans location, but they do not report which of these isomers is the more stable one[8,14].

Previous theoretical studies[2,3,9] demonstrate that although the cyclic six-member systems adopt preferentially a chair conformation, some of them are most stable at the twist conformation. In those theoretical studies on trans isomers of di-and tetrahalogenated of 1,2,4,5-tetroxane it was found that dialogenated molecules prefer isomers trans axial-axial with a chair conformation as the most stable one. Calculations were made at a semiempirical level employing AM1 and PM3 molecular orbital methods[2]. When substituents have not free electron pairs, the trans equatorial-equatorial isomer is the most stable structure. Since there is not available experimental data on these compounds, we present here the conformational analysis of the trans isomers of the glutaldehyde diperoxide (DPG) in order to contribute to complete significant information on 1,2,4,5-tetroxane derivatives.

CALCULATION METHOD

The cost of performing an ab initio Hartree-Fock calculation scales formally as the fourth power of the number of basis functions M. This arises from the number of two - electron integrals necessary for constructing the Fock matrix. Semiempirical methods reduce the computational cost by reducing the number of these integrals. The first step in reducing the computational problem is to consider only the valence electrons implicitly, the core electrons are accounted for by reducing the nuclear charge or introducing functions to model the combined repulsion due to the nuclei and core electrons. The central assumption of semiempirical methods is the Zero Differential Overlap approximation, which neglects all products of basis functions depending on the same electron coordinates when located on different atoms. The neglect of all three-and four-centre two-electron integrals reduces the cinstruction of the Fock matrix from a formal order of M^4 to M^2.

The parametrization of MNDO/AM1/PM3 is performed by adjusting the constants Involved in the different methods so that the results of Hartree-Fock calculations fit experimental data as closely as possible. This fact makes up a suitable circumstance, since the Hartree-Fock lack electron correlation, but the experimental data of course include such effects. This may be viewed as an advantage, the electron correlation effects are implicitly taken into account in

Corresponding Author: Eduardo A. Castro, Inifta, Theoretical Chemistry División, Suc.4, C.C. 16, La Plata 1900, Argentina E-mail: castro@quimica.unlp.edu.ar

The parameterization and we need not perform complicated calculations to improve deficiencies in the Hartree-Fock procedure. Semiempirical methods share the advantage of force field methods, they perform best for systems where much experimental information is already available. The clear advantage of semiempirical procedures over force field techniques is their ability to describe bond breaking and forming reactions.

We resort to the semiempirical AM1 and PM3 methods to calculate the most stable geometrical structures of the title molecule. Among the wide range of possible semiempirical methods, AM1 and PM3 techniques are the most suitable ones and they are usually include in many molecular modeling packages. Results of AM1 and PM3 calculations continue to be reported in the standard chemical literature for a wide variety of applications. AM1 method was proposed in order to surmount well known drawbacks of semiempirical methods to predict hydrogen bonding geometries and energies. PM3 was subsenquently developed with the purpose to improve the optimization of parameters and besides to include a larger set of atoms. At present, both methods continue to be used widely. We have employed the GAUSSIAN 94 package[10].

RESULTS AND DISCUSIÓN

We have calculated the trans a-a and e-e and cis a-e isomers in order to analyze their corresponding relative stabilities and besides we have taken into account the stereoelectronic (anomeric and exoanomeric) effects and their significant role in the trans isomer stability, where both butanal groups are located at the axial position.

Theoretical analysis shows that the trans diaxial isomer is favoured with respect the cis and trans ec-ec isomers and these results are in line with those found for tetroxanes[12] and previous semiempirical calculations[1,2]. In trans isomers there exist a conformational equilibrium between the synclinal and antiperiplanar structures. Below we give information about rotational barriers of the butanal group calculated via both semiempirical methods (i.e. AM1 and PM3 techniques) and we discuss their relative stabilities.

Although the substituent possess free electron pairs, it is somewhat far from oxygen cyclic atoms, but there are effective interactions which are responsible of the higher stability of the trans diaxial-diaxial isomer. This effect can be attributable due to the existence of specific interactions involving the substituent[11], in addition to the own free electron pairs of the oxygen atoms located at the ring.

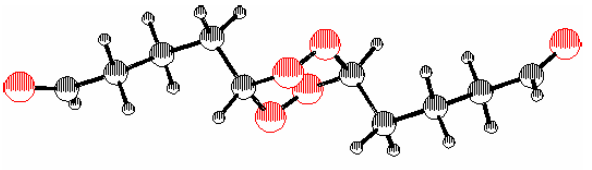


Fig. 1: Trans axial axial 3,6-dibutanal -1,2,4,5-tetroxano

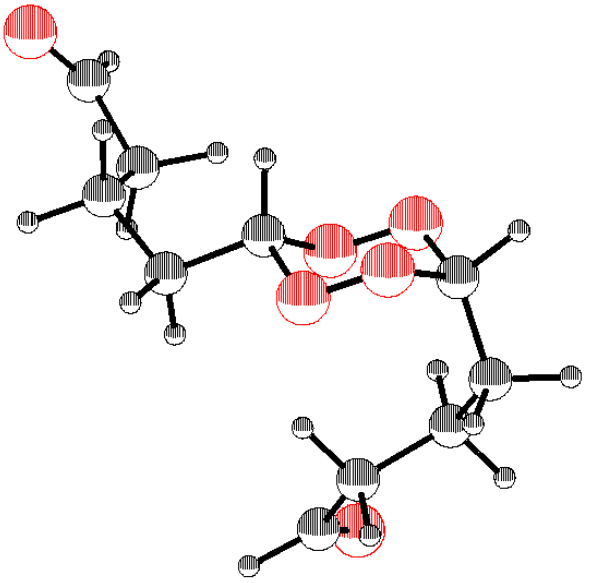


Fig. 2: Cis axial equatorial 3,6-dibutal -1,2,4,5-tetroxane

Table 1: Electronic energy (hartree) of chair isomers of 3, 6-dibutanal-1, 2, 4, 5-tetroxane (DPG)

Isomer		AM1	PM3
trans	a-a	-0.2116681	-0.2267866
cis	a-e	-0.2116212	-0.2200828
trans	e-e	-0.2114365	-0.2116611

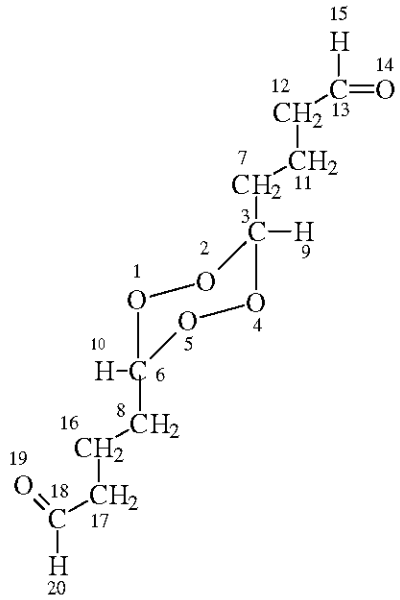
Δ(ΔH) (aa-ee)= 0.15 kcal/mol conversion axial - equatorial (AM1)
Δ(ΔH) (aa-ee)= 9.49 kcal/mol conversion axial - equatorial (PM3)

In Table 1 and Figs. 1, 2 and 3 we display the electronic energies corresponding to the trans a-a and e-e and cis a-e isomers with the chair conformation of 3,6-dibutanal-1,2,4,5-tetroxane. From numerical data we see that the trans axial-axial conformer is the most stable one.

In Table 2 we present the geometrical parameters obtained theoretically from the AM1 and PM3 method. In fact, we give bond lengths, bond angles and dihedral angles for trans and cis isomers of DPG in the chair form. We have not considered the twist structure since the chair one is the most stable one.

The stability order of DPG is analyzed taking into account the following features, which were considered previously in some similar studies[1,12]:

Table 2: Geometrical parameters of trans 3, 6-butanal-1,2,4,5-tetroxano, calculated by semiem-pirical AM1 and PM3 molecular orbital methods



Geometrical parameter	AM1			PM3		
	ax-ax	eq-eq	ax-eq	ax-ax	eq-eq	ax-eq
Bond length (A)						
O_1O_2	1.2940	1.2939	1.2939	1.5694	1.5507	1.5606
O_4O_5	1.2939	1.2938	1.2941	1.5694	1.5504	1.5608
C_6O_5	1.4420	1.4478	1.4425	1.3924	1.4074	1.3941
C_6O_1	1.4421	1.4477	1.4431	1.3923	1.4081	1.3939
C_3O_2	1.4420	1.4478	1.4478	1.3924	1.4073	1.4065
C_3O_4	1.4421	1.4477	1.4472	1.3923	1.4082	1.4053
C_3H_9	1.1215	1.1993	1.1193	1.1222	1.1191	1.1127
C_6H_{10}	1.1215	1.1993	1.1221	1.1222	1.1191	1.1262
C_3C_7	1.5157	1.5168	1.5167	1.5396	1.5436	1.5426
C_7C_{11}	1.5121	1.5122	1.5132	1.5203	1.5207	1.5213
$C_{11}C_{12}$	1.5126	1.5128	1.5131	1.5203	1.5176	1.5200
$C_{12}C_{13}$	1.4987	1.4955	1.4970	1.5089	1.5060	1.5087
$C_{13}O_{14}$	1.2309	1.2312	1.2308	1.2088	1.2092	1.2088
$C_{13}H_{15}$	1.1135	1.1144	1.1030	1.1029	1.1031	1.1028
Bond angle (°)						
$O_2C_3O_4$	102.72	101.93	101.97	105.57	103.42	103.84
$O_1C_6O_5$	102.72	101.94	102.45	105.57	103.42	104.92
$O_2O_1C_6$	112.40	111.09	112.30	108.71	106.95	108.50
$C_6O_5O_4$	112.31	111.27	112.40	108.55	107.13	108.90
$O_5O_4C_3$	112.40	111.09	111.10	108.71	106.95	106.77
$C_3O_2O_1$	112.31	111.28	111.20	108.55	107.13	106.82
$H_9C_3C_7$	114.75	115.52	115.53	111.28	112.21	110.57
$H_{10}C_6C_8$	114.75	115.52	114.69	111.28	112.21	113.05
$H_{15}C_{13}O_{14}$	121.60	121.25	121.46	120.30	119.69	120.32
Torsion angle (°)						
C_6-O_5-O_4-C_3	-64.75	-67.17	-65.92	-65.63	-69.64	-67.44
C_6-O_1-O_2-C_3	64.75	67.16	66.34	65.64	69.64	68.27
O_1-O_2-C_3-O_4	-59.01	-61.51	-61.59	-63.60	-67.08	-67.49
O_4-O_5-C_6-O_1	59.01	61.50	59.11	63.59	67.09	63.83
O_2-O_1-C_6-O_5	-59.07	-61.39	-59.31	-63.70	-67.23	-64.07
O_5-O_4-C_3-O_2	59.07	61.39	61.39	63.70	67.21	67.01

Table: 3: Electronic energy (hartree) of trans diaxial 3, 6-dibutanal-1,2,4,5-tetroxane conformers

Structure	AM1	PM3	ΔH (AM1)	ΔH(PM3)
Synclinal	-0.2116681	-0.2267866	0.0088527	0.0180247
Antiperiplanar	-0.2027856	-0.2087619		

Δ(ΔH) (syn-anti)= 5.56 kcal/mol conversion synclinal-antiperiplanar (AM1)

Δ(ΔH) (syn-anti)= 11.31 kcal/mol conversion synclinal-antiperiplanar (PM3)

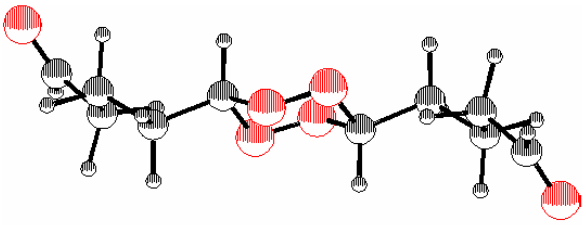


Fig. 3: Trans equatorial equatorial 3, 6-dibutanal-1,2,4,5-tetroxane

- The interaction between adjacent free electron pairs[13], located on the oxygen atoms. In order to discuss this effect, the repulsion between two electrons is considered to follow the order free-pair-free-pair > σ-σ and it reveals itself through anomalous bond angles, specially large deviations of linear bonds of three-center atoms, which usually are considered due to free electron pairs-σ repulsions.
- Torsión angle around O-O bond. Results are shown in Table 2.
- Steric effect, depending of the substituent location at equatorial or axial position[5].
- The anomeric effect that free-electron pairs on endocyclic oxygen atoms exert on the C-Oendo and C-Cexo bonds, when the substituent group is at an axial position.

The rotational barrier of the substituent group around the C(ring)-C(butanal) chemical bond is low (1-3 kcal/mol[11]) and the "exoanomeric" effect must increase this barrier in about an additional amount of 2 kcal/mol. In Table 1 one can see that semiempirical AM1 and PM3 methods predict the trans axial-axial structure is the preferred one, but cis structure is more stable than the trans equatorial-equatorial geometric distribution.

In Table 3 we display the minimum energy data found when a substituent group rotates around the C-Cexo bond, according to both methods. We see synclinal conformer with two anomeric effects and one exo-anomeric effect, is the most stable one and the energy difference between them is 5.5 kcal/mol and 11.3 kcal/mol according to the AM1 y PM3 semiempirical methods, respectively.

Both semiempirical methods show that a shortening of the C-Cexo bond, which is greater for the anti conformer than the synclinal one, which makes clear the stereoelectronic interactions studied here. In the antiperiplanar conformer, C-Oendo bond distances are different but in the synclinal conformer they are similar. For this sort of molecules PM3 method describes in a better manner the changes of C-Oendo and C-Cexo bond lengths.

Regarding the synclinal and antiperiplanar conformers equilibrium, although there is some experimental evidence in quite similar compounds with five member rings (2-metoxi-1,3-dioxolane), that synclinal⇔ antiperiplanar equilibrium in solution phase favors the antiperiplanar form, in these molecule it is found that the most stable conformer is the synclinal one and this result is similar as that found for the 3,6-dimetoxi-1, 2, 4, 5-tetroxane molecule. In DPG theoretical calculations demonstrate that synclinal conformer is the most stable structure because although anti conformer is electronically favoured by stereoelectronic interactions, steric repulsion resulting when butanal substituent is located at an antiperiplanar position regarding the C-H bond, it has as a net effect that the synclinal conformer is the most stable structure.

CONCLUSION

The diaxial conformations for disubtituted molecules of PDG in trans position and the data ΔH>2 kcal/mol for the diaxial-diequatorial equatorial equilibrium should suggest the existence of stereoelectrónic effects contributing to the stabilization of the diaxial conformations of this molecules. Here we have shown that in DPG also the trans diaxial conformations prevail since there is an energy difference larger than 2Kcal/mol between the two trans diaxial- diequatorial conformations.

For this sort of molecules the cis axial ecuatorial structure is the most stable than the trans ecuatorial equatorial one and it is due to the existence of intramolecular interactions leading to a net stabilizing effect in favor of the last structure. In the gauche diaxial conformation there are first-order effects on the C-O bond length, the R-C-O bond angle and the R-C-O-O torsion angles, a shortening of the C-O bond and a lengthening of the adjacent C-O bond as well as an increase of the R-C-O bond angle. These features arise from the PM3 method calculations.

In the cyclic system, while the anomeric effect explains the preference of the axial form with respect to the equatorial one, both show a well defined preference of the substituent, for example, in the butanal grop, to adopt the synclinal form instead that the antiperiplanar one. This is known as an exoanomeric effect. Here we have shown that the cyclic systems studied exhibit both effects and we have to point out that exoanomeric effect is present in both axial and equatorial.conformations.

When substituents are very bulky, the steric effect exceeds the anomeric effect and the more stable conformations are the diequatorial ones A possible explanation for this fact is the change of the R-C-O-O torsion angle, which can avoid the existence of the destabilizing anomeric effect of the diaxial form with respect to the diequatorial one. In the present case this is not the existing situation.

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