Dedicated to the memory of
Professor Maria Brezeanu (1924–2005)

COMPARATIVE STUDY OF SOME IONIC BRIDGES IMPLYING CALCIUM AND MAGNESIUM CATIONS BY COMPUTATIONAL METHODS

Valentin CAREJA,[a] Mircea MRACEC,[a] Ludovic SAYTI,[a] Eugen SISU,[b]
Ramona TUDOSE,[a] and Zeno SIMON[a*]

[a] Institute of Chemistry Timişoara of the Roumanian Academy, 300223-Timişoara, Bd. Mihai Viteazul nr. 24, Roumania
[b] Department of Biochemistry, "V. Babeş" University of Medicine and Pharmacy, 300041-Timişoara, Pţa Eftimie Murgu nr. 2, Roumania

Geometry, electronic structure and energetic calculations were performed with semiempiric and *ab initio* methods of the Hyperchem package for ML_2 and $M^{2+}L_2$ complexes possibly implied in ionic bridges mediating glycan-glycan interactions (M: Ca^{2+} and Mg^{2+}, L: acetate, methylsulphate, etandiol, 1,4-dioxane). Calculated dissociation energies, in vacuum, for ML_2 complexes with anions as ligands are in the range of 400-600 kcal/mol and 150-300 kcal/mol for etheric and alcoholic O-atoms as ligands, by *ab initio* methods. Geometries for acetate ion and 1,4-dioxane, as calculated by *ab initio* methods, are in good agreement with available X-ray crystallographic data.

INTRODUCTION

Ionic bridges with Ca^{2+} and Mg^{2+} cations and $-COO^-$, $-OSO_3^-$, $-OH$, and etheric $-O-$ as Bronstedt basis groups, have important roles in cell recognition and adhesion mediated by glycan-glycan interactions.[1] Studies by computational methods for dissociation energies in water solution of such ML_2 and $M^{2+}L_2$-type complexes were performed by us[2,3] and, for dissociation in vacuum complexes of disaccharides and divalent cations, by Debbaudt, Fereira and Gschaider.[4] It is certainly of interest to study the reliability of computational results for this type of ML_2 and $M^{2+}L_2$ complexes, by comparing calculated and experimental hydration energies[5] and – the subject of this study – to compare experimental and theoretical results (by various methods) for geometry, electronic structure, dissociation energy in vacuum for pertinent ML_2 complexes.

In this paper we perform a systematic study for ML_2 and $M^{2+}L_2$ complexes with acetate, methylsulphate, ethylenediol and dioxane as L-ligands, and Ca^{2+} and Mg^{2+} as cations. The semiempiric ZINDO1 and PM3 methods were used, as well as the *ab initio* method with 3-21G and 6-31G* basis sets of the HyperChem package.[6] Results for geometry, electronic structure, dissociation energy in vacuum, as obtained by different methods, will be compared.

RESULTS

Geometry. Distances and geometries are calculated by *ab initio* 6-31G* for the L-ligands and complexes, for L: acetate (CH_3COO^-), methylsulphate ($CH_3OSO_3^-$), ethyleneglycol ($HOCH_2CH_2OH$) and dioxane

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* Corresponding author: zsimon@acad-icht.tm.edu.ro

$((CH_2CH_2O)_2)$ and Ca^{2+} and Mg^{2+} for M. Comparative results, by ZINDO1, *ab initio* 3-21G and 6-31G*, for M-O and O-central-L-atom bonds are listed in Table 1. For some of the ML_2 and $M^{2+}L_2$ complexes, geometries with lower than maximal symmetry were obtained (*i.e.,* unequal M-O bond lengths), or 0.1 gradient had to be used in order to obtain optimization. As to comparative bond lengths, those obtained by the two *ab initio* variants usually do not differ by more than 0.01 Å, but those obtained by ZINDO1 sometimes differ sensibly (even by 0.5 Å) from the *ab initio* results.

For comparison with bond lengths and geometries from X-ray crystallography, data are available for the CH_3COO^- – anion[7] and for 1,4-dioxane.[8] These data are listed in Table 2 and Table 3 together with results by ZINDO1 and *ab initio* with 3-21G and 6-31G* basis sets. For the acetate anion X-ray data refer to the sodium salt (CH_3COONa).[7] For dioxane, there are two different crystalline structures, above and below 5°C; data for both structures are given together with corrections for zero point vibrations.[8]

Table 1

Geometry data for L-ligands and complexes calculated by ZINDO1 and by *ab initio* with 3-21G and 6-31G* basis sets. M-O: metal-oxygen atom distance; C-O(S-O): oxygen-central ligand atom (C or S) distance (Å); *geometry with lower than maximal symmetry (unequal M-O bonds), possible effect of unsuccessful optimization; ☐ (cassette): results obtained with 0.1 gradient; CH_3COO^- acetate, $CH_3OSO_3^-$ methylsulphate, $(CH_2OH)_2$ ethyleneglicol, $(CH_2CH_2O)_2$ 1,4-dioxane

bond	C-O (S-O)			M-O		
method	ZINDO1	3-21G	6-31G*	ZINDO1	3-21G	6-31G*
CH_3COO^-	1.3	1.24	1.23	-	-	-
$(CH_3COO)_2Ca$	1.311	1.272	1.252	2.758	2.333	2.343
$(CH_3COO)_2Mg$	1.284/1.343*	1.279	1.254	2.22/3.44*	1.994	2.005
$CH_3OSO_3^-$	1.741	1.555/1.560	1.438/1.446	-	-	-
$(CH_3OSO_3)_2Ca$	1.744	1.54/1.59*	1.45	2.900	2.45/4.2*	2.52/2.79
$(CH_3OSO_3)_2Mg$	1.766	1.55/1.60*	1.41/1.49*	2.338	1.99/3.89*	2.03/3.4*
$(CH_2OH)_2$	1.390	1.441	1.402	-	-	-
$((CH_2OH)_2)_2Ca$	1.400	1.481	1.445	2.801	2.311	2.381
$((CH_2OH)_2)_2Mg$	1.389*	1.489	1.454	2.900*	1.938	2.001
$(CH_2CH_2O)_2$	1.393	1.444	1.401	-	-	-
$((CH_2CH_2O)_2)_2Ca$	1.401	1.472	1.431	2.869	2.370	2.438
$((CH_2CH_2O)_2)_2Mg$	1.397*	1.486	1.447	2.922*	1.985	2.031

Ab initio results are generally more near to experimental results (see Tables 2 and 3) than those of ZINDO1 calculations. Small differences in bond lengths, as compared to those expected for maximal symmetry in X-ray results should be attributed to the influence of crystalline lattice.

For chair, 1,4-dioxane, both X-ray data[8] and our *ab initio* calculations indicate a slightly twisted structure for the C_4-quasiplan.

Table 2

X-ray crystallography data for the CH_3COO^- – anion (in CH_3COONa),[7] C1, O1, O2 – atoms of the carboxylate, C2, H1, H2, H3 – atoms of the methyl group. First column, experimental results, columns 2-4 results of ZINDO1, *ab initio* 3-21G and 6-31G* calculations (Å)

bond	experimental	acetate		
		ZINDO1	3-21G	6-31G*
O1-C1	1.245	1.306	1.248	1.233
O2-C1	1.255	1.307	1.251	1.235
C1-C2	1.511	1.48	1.575	1.553
C2-H1	0.916	1.098	1.086	1.085
C2-H2	0.915	1.098	1.086	1.088
C2-H3	1.05	1.098	1.086	1.088

Table 3

X-ray crystallography data for 1,4-dioxane[8]. C-O bonds: O1-C2, O1-C6; C-C bond:C2-C3; C-H bonds: C2H21, C2-H22, C6-H61, C6-H62. B I – structure stable below 5°C, B II – above 5°C. In parentheses, data corrected for zero point vibrations. Last three columns – results from ZINDO1, *ab initio* 3-21G and 6-31G* calculations (Å)

bond	B I	B II	ZINDO1	3-21G	6-31G*
O1-C2	1.423 (1.445)	1.432 (1.441)	1.394	1.444	1.402
O1-C6	1.426 (1.446)	1.429 (1.436)	1.394	1.444	1.402
C2-C3	1.478 (1.495)	1.513 (1.522)	1.486	1.523	1.518
C2-H21	1.02	0.97	1.104	1.079	1.082
C2-H22	1.03	0.98	1.104	1.084	1.089
C6-H61	1.02	1.00	1.104	1.079	1.082
C6-H62	0.95	0.97	1.104	1.084	1.089

Electronic structure. Atomic charges for the central M-atom and the M-binding O or S atoms of the L-ligands, as calculated by ZINDO1, *ab initio* 3-21G and 6-31G* are listed in Table 4. The difference between 3-21G and 6-31G* is rather small. ZINDO1 results differ rather significantly from *ab initio* results; O-atom charges are significantly less negative than the *ab initio* ones, M-atom charges are significantly less positive.

Some differences between the equivalence of the four M-O or M-S bonds within the complexes may be the result of the 0.1 RMS gradient.

Table 4

Electronic charges (electron units) of central M atom and chelating O atom, calculated by ZINDO1, *ab initio* 3-21G and 6-31G*

atom	O			M		
method	ZINDO1	3-21G	6-31G*	ZINDO1	3-21G	6-31G*
CH_3COO^-	-0.64	-0.80	-0.77	-	-	-
$(CH_3COO)_2Ca$	-0.51	-0.802	-0.771	1.012	1.48	1.428
$(CH_3COO)_2Mg$	-0.44*	-0.752	-0.749	0.391*	1.148	1.076
$CH_3OSO_3^-$	-0.505	-0.819/-0.846	-0.752/-0.791	-	-	-
$(CH_3OSO_3)_2Ca$	-0.428/-0.439	-0.70/-0.88*	-0.758/-0.824	1.276	1.456	1.340
$(CH_3OSO_3)_2Mg$	-0.34	-0.815/-0.695	-0.65/-0.82*	0.653	1.095	1.035
$(CH_2OH)_2$	-0.341	-0.691	-0.748	-	-	-
$((CH_2OH)_2)_2Ca$	-0.351	-0.802	-0.901	1.468	1.620	1.636
$((CH_2OH)_2)_2Mg$	-0.310*	-0.798	-0.911	0.447	1.351	1.468
$(CH_2CH_2O)_2$	-0.274	-0.635	-0.657	-	-	-
$((CH_2CH_2O)_2)_2Ca$	-0.263	-0.703	-0.735	1.508	1.680	1.643
$((CH_2CH_2O)_2)_2Mg$	-0.190*	-0.680	-0.737	0.435	1.354	1.358

Energetic results. Computed heats of formation can be compared with experimental ones (first plus second ionization potentials[9]) for Ca^{2+} and Mg^{2+}. Heats of formation, computed by *ab initio* 3-21G, 6-31G*, ZINDO1 and PM3 are for Ca^{2+} (kcal/mol) 378; 379; 473; 433; experimental 412, while for Mg^{2+}: 489; 491; 566; 555; experimental 519.

Results for dissociation energies of ML_2 complexes (vacuum) are listed in Table 5.

Again dissociation energies calculated by *ab initio* methods (3-21G and 6-31G*) generally differ less between themselves than from those calculated by ZINDO1. The highest dissociation energy is for the Mg-acetate-ML_2 complex for all three methods. In 3-21G the decreasing order is L: acetate, methylsulphate, ethyleneglycol, dioxane and Mg^{2+}-complexes are more stable than the corresponding Ca^{2+}-complexes. For 6-31G*, there is a single inversion (Mg-methylsulphate more stable than Ca-acetate), but for ZINDO1 all

Mg-complexes have higher dissociation energies than the Ca-complexes. Dissociation energies calculated (single point) with ZINDO1 and PM3, starting from 3-21G or 6-31G* geometries are strongly method-dependent and present also significant differences as compared to those calculated by *ab initio* methods.

Table 5

Dissociation energies (kcal/mol) for ML_2 complexes (($ML_2 \longrightarrow 2L + M$, vacuum). Results of ZINDO1, *ab initio* 3-21G and 6-31G*, and single point calculations by ZINDO1 and PM3 with *ab initio* geometries. Legend – see Table 1

method	3-21G+ ZINDO1	3-21G+ PM3	6-31G*+ ZINDO1	6-31G*+ PM3	ZINDO1	3-21G	6-31G*
$(CH_3COO)_2Ca$	451.94	636.59	447.10	634.63	542.82	522.13	509.61
$(CH_3COO)_2Mg$	885.79	578.02	876.95	570.73	1012.15*	645.72	612.99
$(CH_3OSO_3)_2Ca$	423.30*	578.35*	365.40	602.90	466.06	447.85*	428.38
$(CH_3OSO_3)_2Mg$	785.72*	506.08*	778.38*	481.64*	870.51	588.19*	529.22*
$((CH_2OH)_2)_2Ca$	11.79	376.64	61.50	362.34	152.25	226.45	184.79
$((CH_2OH)_2)_2Mg$	410.47	191.62	450.51	170.45	613.76*	342.01	270.67
$((CH_2CH_2O)_2)_2Ca$	-31.17	441.02	18.42	440.22	121.68	170.29	136.80
$((CH_2CH_2O)_2)_2Mg$	417.48	135.72	464.26	133.36	742.44	281.57	218.27

Dissociation energies for our complexes, those calculated by the *ab initio* 6-31G* method are in the range of 400-600 kcal/mol for anionic L-ligands and lower, 150-300 kcal/mol for neutral L-ligands, higher for Mg^{2+} than for the corresponding Ca^{2+} complexes; both trends are in agreement with expectations from heuristic consideration. For chitosan-Hg^{2+}, Pb^{2+}, Cd^{2+} complexes, according to MM2-PM3 results,[4] dissociation energies are in the range of 200-500 kcal/mol, *i.e.*, the same range as our results.

DISCUSSION

Geometries and electronic structures calculated by *ab initio* 3-21G and 6-31G* methods seem to be more reliable than those calculated by the semiempiric ZINDO1 method, at least when no geometries with lower symmetry are implied. The last cases could imply optimization above the 0.01 gradient. Results obtained by the most advanced *ab initio* 6-31G* method can be recommended. When the available X-ray data geometries are compared with the calculated ones, the *ab initio* methods give better results than the semiempiric ZINDO1 method. For these X-ray data, the 3-21G basis set seems even to give better results than the 6-31G* basis set.

METHOD

Geometry and electronic structures of L-ligands and ML_2 and $M^{2+}L_2$-complexes were computed by the *ab initio* method with 3-21G and 6-31G* basis sets and with the semiempirical ZINDO1 and PM3 methods of the HyperChem package.[6] Dissociation energies for the $ML_2 \longrightarrow 2L^- + M^{2+}$ and $M^{2+}L_2 \longrightarrow 2L + M^{2+}$ processes (vacuum) were calculated by these methods (from total electronic energies), but also by the single point method with ZINDO1 and PM3, starting from geometries calculated by the two *ab initio* variants. A 0.01 RMS gradient was used; however, in several cases, a 0.1 RMS gradient was used, because a 0.01 RMS gradient was not attained.

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