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Conformational analysis of the isomers of lewisite†

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ABSTRACT: Chlorovinyldichloroarsine, also known as lewisite, is a powerful vesicant that has been used in the past as a chemical weapon. Its extreme toxicity makes obtaining experimental data to characterize this notorious chemical system very challenging. In this work, *ab initio* calculations were carried out on the *geminal*, *cis* and *trans* isomers of lewisite at a variety of levels of theory employing both all-electron and effective-core potential basis sets. The aims were to ascertain the relative stability of these three isomeric forms of lewisite and to characterize their structures, dipole moments and conformational preferences. The *trans* isomer of lewisite was found to be the most stable and the geminal isomer the least stable. This is consistent with the experimental data available on the compositions of lewisite mixtures. Copyright © 1999 John Wiley & Sons, Ltd.

KEYWORDS: lewisite; 2-chlorovinyldichloroarsine; conformational analysis

INTRODUCTION

The compound *trans*-2-chlorovinyldichloroarsine (lewisite), a powerful blistering agent first produced near the end of World War I, is capable of inflicting severe chemical burns of the eyes, skin and lungs.[1] Bioassays and toxicological studies of lewisite are complicated by the fact that typical preparations contain a mixture of products including *trans*-2-chlorovinyldichloroarsine (lewisite), *cis*-2-chlorovinyldichloroarsine (isolewisite or *cis*-lewisite) and 1-chlorovinyldichloroarsine (*geminal* lewisite) (Fig. 1). The major component of lewisite is the *trans* isomer (*ca* 95%), and the presence of the geminal isomer was only recently detected.[2] Lewisite is prepared by the reaction of acetylene with arsenic trichloride, which produces a mixture of the products shown in Fig. 1 and also bis(2-chlorovinyl)chloroarsine and tris(2-chlorovinyl)arsine.[3]

The determination of the chemical properties of the various isomers of lewisite can aid in understanding data from the screening of possible lewisite antidotes. Also, this information can potentially lead to identifying whether a specific isomer of lewisite causes the vesicant injury. The ability to determine the isomeric ratio of a lewisite sample is useful as a method to assay purity. Currently, purity can be determined through the use of NMR spectroscopy via analysis of ^{1}H–^{1}H coupling constants. Small amounts of the geminal isomer have also been studied by gas chromatography–mass spectrometry and infrared spectroscopy.[2] Early methods to characterize the isomers focused on the dipole moment. In 1938, lewisite was reported to have a dipole moment of 1.77 D in benzene.[4] The exact structure was not given but has been assumed to be the *trans* isomer.[5] In 1948, McDowell *et al.*[5] used a group-additive approach to estimate the dipole moments of the isomers to be 2.03 D for the *trans*, 2.14 or 3.20 D for the *cis* (depending on the extent of free rotation about the C—As bond) and 1.15 for the *geminal* isomer.[5]

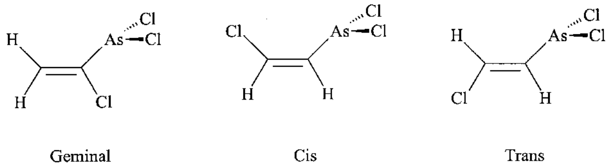

Figure 1. *Geminal*, *cis* and *trans* isomers of lewisite.

The current work is, to our knowledge, the first application of *ab initio* molecular orbital methods to the study of the isomers of lewisite. There is an obvious advantage to the application of computational methods to this highly toxic system. The goal of this work was to determine the relative stability of the isomers, which first requires a determination of the preferred conformation (Fig. 2) for each. Also, these calculations allow for

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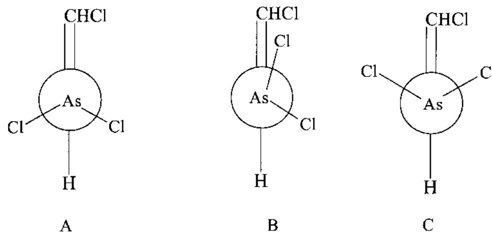

Figure 2. A, B and C, conformations of lewisite. The view is along the As—C bond showing the position of the $AsCl_2$ group in relation to the approximate plane of the C=C bond.

the structural characterization of each of the isomers and an estimate of their dipole moments. We employed both all-electron and effective core potential basis sets and examined the effect of electron correlation in each case.

METHODS

All *ab initio* calculations were carried out with the Gaussian 94 program.[6] Initial geometries were created and computational results were visualized by using the Spartan[7] program package as the graphical front-end to Gaussian 94. Our initial geometry optimizations were of conformers A and C (see Fig. 2) and were constrained to C_s symmetry at the HF/LANL2DZ level of theory.[8] The LANL2DZ basis set as implemented in the Gaussian 94 program employs Dunning *et al.*'s D95 basis[9] for first-row elements and the Los Alamos effective core potential plus DZ on heavier elements. Upon release of the symmetry constraints, reoptimization led in some cases to conformer B. The use of other C—As bond rotamers as starting geometries produced no additional conformers. All stationary points were characterized and zero-point vibrational energies were determined with frequency calculations at the HF/LANL2DZ//HF/LANL2DZ level. Electron correlation was included with second-order Møller–Plesset[10] perturbation theory in geometry optimizations of conformers A, B and C at the MP2/LANL2DZ level. Geometry optimizations were also carried out at the HF/6–311+G(2d,p) and MP2/6–311+G(2d,p) levels with characterization of stationary points by frequency calculations performed at the HF/6–311+G(2d,p)//HF/6–311+G(2d,p) level.

RESULTS AND DISCUSSION

Structures

Tables 1–4 contain selected structural features of the various conformers of the *geminal*, *cis* and *trans* isomers of lewisite. At the HF/LANL2DZ//HF/LANL2DZ level the C conformations for the *geminal* and *trans* isomers were identified as transition states by the presence of one imaginary frequency. For the *geminal* and *trans* isomers, when input structures were created by rotating the C—As bond slightly to produce a conformation of C_1 symmetry, geometry optimization led to the twisted conformation B. For the *cis* isomer, this procedure produced conformation A or C upon geometry reoptimization.

Several trends emerge on comparing the HF/LANL2DZ geometries (Table 1) with the HF/6–311+G(2d,p) geometries (Table 3). Overall, the calculated bond lengths are longer with the HF/LANL2DZ effective core potential than those calculated with the all-electron HF/6–311+G(2d,p) basis set. The bond angles are very similar for the two basis sets (within 2°). For the twisted conformation B, the $AsCl_2$ moiety is twisted slightly more out of the approximate plane of the vinyl group with HF/LANL2DZ than with HF/6–311+G(2d,p). This is evidenced by the C=C—As—$AsCl_2$ dihedral angle, where $AsCl_2$ represents the centroid of the $AsCl_2$ group. This dihedral angle is 47.2° at the HF/LANL2DZ level and 57.2° at the HF/6–311+G(2d,p) level for the *geminal* isomer and 61.2° and 68.2° [at the HF/LANL2DZ and HF/6-311+G(2d,p) levels,respectively] for the *trans* isomer.

The data in Tables 1–4 also allow for an evaluation of the effect of including electron correlation at the MP2 level in the effective core and all-electron cases on the calculated structures. Comparison of Tables 1 and 2 reveals that for LANL2DZ longer bond lengths are calculated when electron correlation is included in the geometry optimization. There is little change in the bond angles upon inclusion of electron correlation for LANL2DZ, and there is only a slight increase in the C=C—As—$AsCl_2$ dihedral angle. In general, the inclusion of electron correlation with MP2 has less of an impact for the 6–311+G(2d,p) basis set (Tables 3 and 4). In most cases, there are only slight changes in the geometrical parameters for the MP2/6–311+G(2d,p) structures as compared with the HF/6–311+G(2d,p) structures. The largest effect is seen for the C=C bond length, which increases by approximately 0.02 Å for the MP2/6–311+G(2d,p) structures.

The *trans* isomer of lewisite has been examined experimentally via gas-phase electron diffraction by Pronicheva *et al.*[11] They reported the following structural parameters: C=C 1.374 Å, As—C 1.891 Å, As—Cl 2.197 Å, C—Cl 1.729 Å, C—H 0.961, CCAs 121.0°, CCCl 121.3°, CAsCl 101.1°, ClAsCl 99.1°, CCH 127.8° and a C=C—As—$AsCl_2$ dihedral angle of 162.1°. The conformation in this experimental determination is closest to A in the work reported here (where the C=C—As—$AsCl_2$ dihedral angle is 180°). Interestingly the C=C bond length of 1.374 Å is significantly longer than that predicted by any of the calculations performed here. It is also much longer than the values that have been measured or assumed (based on *ab initio* MO calculations) in microwave spectroscopic studies of similar

Table 1. Selected geometrical features calculated at the HF/LANL2DZ//HF/LANL2DZ level

Compound	Conformer[a]	C—Cl[b]	C=C[b]	C—As[b]	As—Cl[b,c]	C=C—As[d]	C—As—Cl[d]	Cl—As—Cl[d]	C=C—As—$AsCl_2$[e]
Geminal	A (0)	1.794	1.330	1.954	2.278	119.0	98.6	98.9	180.0
	B (0)	1.822	1.324	1.959	2.291 2.291	130.1	97.3 97.3	98.7	47.2
	C (1)	1.822	1.324	1.962	2.291	128.9	97.6	97.2	0.0
Cis	A (0)	1.797	1.324	1.949	2.292	125.4	94.8	98.0	180.0
	C (0)	1.775	1.327	1.947	2.287	133.9	100.2	99.9	0.0
Trans	A (0)	1.788	1.325	1.942	2.288	119.9	96.1	98.0	180.0
	B (0)	1.791	1.324	1.945	2.291 2.296	126.6	98.4	100.0	61.2
	C (1)	1.788	1.324	1.947	2.295	125.6	98.5	97.3	0.0

[a] See Fig. 2 for conformer definitions. The number in parentheses represents the number of imaginary frequencies calculated at the HF/LANL2DZ//HF/LANL2DZ level.

[b] Distances in Å.

[c] For conformer B the two As—Cl bonds are not symmetry equivalent. The top values for the As—Cl bond length and C—As—Cl angle pertain to the As—Cl bond that is most eclipsed with the C=C bond and the bottom values pertain to the As—Cl bond that is most out of plane with respect to the C=C bond.

[d] Bond angles in degrees.

[e] This parameter is the dihedral angle (in degrees) associated with C—As bond rotation. It is measured as C=C—As—X, where X is the centroid of the $AsCl_2$ fragment.

Table 2. Selected geometrical features Calculated at the MP2/LANL2DZ//MP2/LANL2DZ level

Compound	Conformer[a]	C—Cl[b]	C=C[b]	C—As[b]	As—Cl[b,c]	C=C—As[d]	C—As—Cl[c,d]	Cl—As—Cl[d]	C=C—As—$AsCl_2$[e]
Geminal	A (0)	1.824	1.367	1.987	2.318	117.9	97.8	99.5	180.0
	B (0)	1.850	1.361	1.994	2.327 2.327	129.1	97.0 96.6	100.0	56.2
	C (1)	1.849	1.361	1.999	2.329	127.9	96.8	98.2	0.0
Cis	A (0)	1.829	1.362	1.976	2.330	125.1	94.2	98.5	180.0
	C (0)	1.808	1.366	1.975	2.328	133.8	99.5	100.2	0.0
Trans	A (0)	1.820	1.363	1.972	2.329	119.7	95.3	98.5	180.0
	B (0)	1.824	1.362	1.972	2.331 2.335	125.9	97.6 95.6	101.5	68.6
	C (1)	1.822	1.362	1.977	2.334	124.9	97.6	97.8	0.0

[a–e] See Table 1.

Table 3. Selected geometrical features calculated at the HF/6–311+G(2d,p)//HF/6–311+G(2d,p) level

Compound	Conformer[a]	C—Cl[b]	C=C[b]	C—As[b]	As—Cl[b,c]	C=C—As[d]	C—As—Cl[c,d]	Cl—As—Cl[d]	C=C—As—$AsCl_2$[e]
Geminal	A (0)	1.732	1.314	1.942	2.175	117.3	99.1	99.2	180.0
	B (0)	1.752	1.309	1.949	2.182 2.181	128.5	99.2 97.6	99.2	57.2
	C (0)	1.753	1.308	1.957	2.185	127.2	98.4	98.4	0.0
Cis	A (0)	1.737	1.310	1.934	2.188	124.5	95.9	98.6	180.0
	C (0)	1.722	1.312	1.940	2.182	133.3	100.7	99.9	0.0
Trans	A (0)	1.731	1.311	1.925	2.184	118.0	97.4	98.6	180.0
	B (0)	1.735	1.309	1.932	2.183 2.188	125.5	99.9 96.9	100.0	68.2
	C (1)	1.732	1.308	1.938	2.187	124.6	99.5	98.3	180.0

[a] See Fig. 2 for conformer definitions. The number in parentheses represents the number of imaginary frequencies calculated at the HF/6–311+G(2d,p)//HF/6–311+G(2d,p) level.
[b–e] See Table 1.

Table 4. Selected geometrical features calculated at the MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p) level

Compound	Conformer[a]	C—Cl[b]	C=C[b]	C—As[b]	As—Cl[b,c]	C=C—As[d]	C—As—Cl[c,d]	Cl—As—Cl[d]	C=C—As—$AsCl_2$[e]
Geminal	A (0)	1.734	1.337	1.950	2.189	116.9	97.3	99.2	180.0
	B (0)	1.751	1.332	1.955	2.195 2.195	128.0	98.1 95.8	99.6	60.4
	C (0)	1.751	1.331	1.964	2.197	126.4	97.1	98.6	0.0
Cis	A (0)	1.742	1.333	1.936	2.202	123.1	94.7	98.7	180.0
	C (0)	1.724	1.337	1.941	2.197	131.7	99.1	100.0	0.0
Trans	A (0)	1.733	1.334	1.926	2.198	117.1	96.2	98.6	180.0
	B (0)	1.736	1.333	1.933	2.197 2.203	124.4	98.5 95.6	100.3	70.1
	C (1)	1.734	1.333	1.940	2.202	122.8	97.9	98.1	180.0

[a–e] See Table 3.

Table 5. Calculated relative conformational energies for lewisite isomers

		Conformation					
		A		B		C	
Compound	Method	ΔE[a]	$\Delta E + \Delta ZPE$[b]	ΔE	$\Delta E + \Delta ZPE$	ΔE	$\Delta E + \Delta ZPE$
Geminal	HF/LANL2DZ//HF/LANL2DZ	1.66	1.71[c]	0.00	0.00[c]	1.01	0.86[c]
	MP2/LANL2DZ//MP2/LANL2DZ	0.87	0.92[c]	0.00	0.00[c]	1.31	1.16[c]
	HF/6–311+G(2d,p)//HF/6–311+G(2d,p)	0.00	0.00[d]	0.23	0.20[d]	1.96	1.75[d]
	MP2/6–311+G(2d,p)//MP2/LANL2DZ	0.00	0.00[c]	0.51	0.45[c]	2.05	1.85[c]
	MP2/6–311+G(2d,p)//HF/6–311+G(2d,p)	0.00	0.00[d]	0.27	0.24[d]	2.00	1.79[d]
	MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p)	0.00	0.00	0.27	0.24	2.01	1.81
Cis	HF/LANL2DZ//HF/LANL2DZ	0.00	0.00[c]			5.46	5.55[c]
	MP2/LANL2DZ//MP2/LANL2DZ	0.00	0.00[c]			4.53	4.61[c]
	HF/6–311+G(2d,p)//HF/6–311+G(2d,p)	0.00	0.00[d]			5.52	5.55[d]
	MP2/6–311+G(2d,p)//MP2/LANL2DZ	0.00	0.00[c]			3.93	4.01[c]
	MP2/6–311+G(2d,p)//HF/6–311+G(2d,p)	0.00	0.00[d]			4.02	4.05[d]
	MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p)	0.00	0.00			3.84	3.87
Trans	HF/LANL2DZ//HF/LANL2DZ	0.00	0.00[c]	0.17	0.21[c]	1.30	1.17[c]
	MP2/LANL2DZ//MP2/LANL2DZ	0.35	0.31[c]	0.00	0.00[c]	1.49	1.32[c]
	HF/6–311+G(2d,p)//HF/6–311+G(2d,p)	0.00	0.00[d]	1.71	1.71[d]	3.33	3.15[d]
	MP2/6–311+G(2d,p)//MP2/LANL2DZ	0.00	0.00[c]	0.83	0.87[c]	2.07	1.94[c]
	MP2/6–311+G(2d,p)//HF/6–311+G(2d,p)	0.00	0.00[d]	0.93	0.93[d]	2.23	2.05[d]
	MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p)	0.00	0.00	1.50	1.50	2.10	1.92

[a] Conformational energy differences in kcal mol^{-1}.

[b] Conformational energy differences, corrected for differences in zero-point vibrational energy, in kcal mol^{-1}.

[c] Zero-point vibrational energies calculated at the HF/LANL2DZ//HF/LANL2DZ level.

[d] Zero-point vibrational energies calculated at the HF/6–311+G(2d,p)//HF/6–311+G(2d,p) level.

substituted ethylenes (e.g., 1.339 Å for ethylene,[12] 1.324 Å for vinylamine[13] and 1.3211 Å for vinylphosphine[14]). The best agreement for the C=C bond length with the gas-phase electron diffraction data is obtained with MP2/LANL2DZ with a value of 1.363 Å for the low-energy conformation of *trans*-lewisite. MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p) predicts a value of 1.334 Å for the C=C bond length. It is noteworthy that there is a 0.04 Å difference between the experimental and MP2/6–311+G(2d,p) values given that this computational protocol results in very good agreement with the experimental C=C bond lengths in more typical ethylenes (e.g. 1.334 Å calculated with MP2/6–311+G(2d,p) for ethylene versus the experimental value of 1.339 Å[12] and 1.332 Å for vinylamine versus 1.325 Å[13]). The best agreement between the calculated and experimental structure is observed for the structural parameters that involve the As and Cl. For example, the experimental Cl—As—Cl bond angle of 99.1° is well represented by all of the computational methods. The experimental As—Cl distance of 2.197 Å is very accurately reproduced by MP/6–311+G(2d,p) with a value of 2.198 for the lowest energy conformation of the *trans* isomer. Thus, the highest level of theory used here, MP2/6–311+G(2d,p), produces As—Cl bond lengths and Cl—As—Cl bond angles that are in very close agreement with the experimental values for *trans*-lewisite. This raises the question of why is there not better agreement with the experimental C=C bond distance for *trans*-lewisite given that MP2/6–311+G(2d,p) has an established track record of predicting accurate structures for other substituted ethylenes. The answer may lie in the fact that the experimental structure was determined using gas-phase electron diffraction and one might expect more precise measurements for structural parameters involving the heavier As and Cl atoms with their large electron densities. The details of the underlying C=C framework are perhaps masked from experimental diffraction techniques by the presence of the large Cl and $AsCl_2$ groups attached to the periphery of the molecule.

Conformational energies

The calculated conformational energies for each of the lewisite isomers are presented in Table 5. For the *geminal* isomer, conformation B is the lowest in energy with the HF/LANL2DZ//HF/LANL2DZ and MP2/LANL2DZ//MP2/LANL2DZ methods, whereas all of the other computational protocols predict conformation A to be the lowest in energy. However, the twisted conformation B is calculated to be only slightly higher in energy. In all cases, differences in zero-point vibrational energies are minimal. Electron correlation has a much more dramatic effect when comparing the results obtained with HF/LANL2DZ//HF/LANL2DZ with those obtained with MP2/LANL2DZ//MP2/LANL2DZ than is seen with the

Table 6. Calculated relative energies of lewisite isomers

	Isomer					
	Geminal		*Cis*		*Trans*	
Method	ΔE[a]	$\Delta E + \Delta ZPE$[b]	ΔE	$\Delta E + \Delta ZPE$	ΔE	$\Delta E + \Delta ZPE$
HF/LANL2DZ//HF/LANL2DZ	2.84	2.67[c]	0.00	0.00[c]	0.15	0.12[c]
MP2/LANL2DZ//MP2/LANL2DZ	1.93	1.75[c]	0.02	0.01[c]	0.00	0.00[c]
HF/6–311+G(2d,p)//HF/6–311+G(2d,p)	3.89	3.79[d]	1.40	1.41[d]	0.00	0.00[d]
MP2/6–311+G(2d,p)//MP2/LANL2DZ	1.35	1.26[c]	0.52	0.55[c]	0.00	0.00[c]
MP2/6–311+G(2d,p)//HF/6–311+G(2d,p)	1.26	1.16[d]	0.63	0.64[d]	0.00	0.00[d]
MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p)	1.22	1.12[d]	0.59	0.61[d]	0.00	0.00[d]

[a] Relative energies of the isomers of lewisite (the differences in total energies for the most stable conformation of each isomer), in kcal mol^{-1}.
[b] Relative energies of the isomers of lewisite corrected for differences in zero-point vibrational energies, in kcal mol^{-1}.
[c] Zero-point vibrational energies calculated at the HF/LANL2DZ//HF/LANL2DZ level.
[d] Zero-point vibrational energies calculated at the HF/6–311+G(2d,p)//HF/6–311+G(2d,p) level.

all-electron calculations. Electron correlation at the MP2 level has little effect on the conformational energy differences when the HF/6–311+G(2d,p) basis set is used. Also, the MP2/6–311+G(2d,p) conformational energies at the HF/6–311+G(2d,p) geometries are nearly identical with those calculated at the MP2/6–311+G(2d,p) geometries. The differences are larger, although still less than 0.3 kcal mol^{-1} (1 kcal = 4.184 kJ), if the MP2/LANL2DZ geometry is used.

For the *cis* isomer, a minimum was not found in the region of conformation B. Input structures with the B conformation moved upon geometry optimization to conformation A or C. Presumably this is due to Cl—Cl repulsion between the $AsCl_2$ group and the vinyl chloro group. By all methods, conformation C is calculated to be higher in energy than A by values ranging from 3.84 to 5.52 kcal mol^{-1}. Once again, zero-point energy corrections make little difference to the conformational energies. The inclusion of electron correlation in the calculation of the geometry optimization acts to decrease the energy of the C conformation relative to that of A for both the effective core potential and the all-electron basis sets.

For the *trans* isomer, the A conformation is the lowest in energy for all methods except MP2/LANL2DZ//MP2/LANL2DZ, by which it is predicted to lie 0.31 kcal mol^{-1} (with zero-point energy corrections) above conformation B. For all of the other methods, the conformations are ranked in order of increasing energy as $A < B < C$. The greatest spread of energies is predicted by HF/6–311+G(2d,p)//HF/6–311+G(2d,p), for which conformation C is 3.15 kcal mol^{-1} higher in energy than A. The inclusion of electron correlation in the calculation, and whether it is included only in the energy or also in the geometry optimization, appears to be a larger factor for the *trans* than for the *geminal* or *cis* isomer. For all three isomers, the most sophisticated levels of theory used in this study identify conformation A as the lowest in energy. For the *geminal* isomer, however, there is only a very small preference for conformation A.

Relative stabilities of the isomers

As stated above, the preparation of lewisite by the reaction of $AsCl_3$ and acetylene leads to a mixture of isomeric products comprised mainly of the *trans* isomer, a lesser amount of the *cis* isomer and only a negligible amount of the *geminal* isomer. Presumably, this product mixture is representative of the relative thermodynamic stability of each of the isomers, although it could also be the result of a combination of other effects including kinetics, solubility or preparation procedures. To address this point, we compared the absolute energies of the most stable conformation for each of the lewisite isomers. The relative isomeric energies are presented in Table 6. The results in Table 6 lead to the conclusion that the product ratios typically encountered in lewisite preparations are reflective of the relative thermodynamic stability of the three isomers. The comparison of the most favored conformation of each isomer at the MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p) level results in a preference for the *trans* isomer of approximately 0.6 kcal mol^{-1} over the *cis* isomer and over 1 kcal mol^{-1} for the *geminal* isomer. All of the computational protocols predict the *geminal* isomer to be the least stable isomer of lewisite. All of the methods predict the *trans* isomer to be the most stable with the single exception of the HF/LANL2DZ//HF/LANL2DZ protocol, which predicts a very slight preference for the *cis* over the *trans* isomer. Presumably, the instability of the *geminal* isomer results from the combination of unfavorable steric and electrostatic interactions due to the close proximity of the vinyl chloro and $AsCl_2$ groups, which is not a factor in the *cis* and *trans* isomers. Analysis of space-filling models of the conformations of the *geminal* isomer reveals close Cl…Cl contacts in the A conformation and close Cl…H

Table 7. Calculated dipole moments (D) of lewisite isomers

		Conformer		
Compound	Method	A	B	C
Geminal	HF/LANL2DZ//HF/LANL2DZ	5.899	3.216	2.203
	MP2/LANL2DZ//MP2/LANL2DZ	4.758	2.778	1.797
	HF/6–311+G(2d,p)//HF/6–311+G(2d,p)	3.444	2.120	1.480
	MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p)	3.015	1.853	1.212
Cis	HF/LANL2DZ//HF/LANL2DZ	3.541		5.782
	MP2/LANL2DZ//MP2/LANL2DZ	3.021		4.940
	HF/6–311+G(2d,p)//HF/6–311+G(2d,p)	2.517		3.456
	MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p)	2.358		3.130
Trans	HF/LANL2DZ//HF/LANL2DZ	3.873	3.421	3.290
	MP2/LANL2DZ//MP2/LANL2DZ	3.325	2.970	2.966
	HF/6–311+G(2d,p)//HF/6–311+G(2d,p)	2.102	1.752	1.757
	MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p)	2.229	1.733	1.769

contacts in the B conformation. The only conformation of this isomer that escapes these close contacts is the C conformation, which contains an eclipsing interaction between the As lone pair and the C—Cl bond.

Dipole moments

As stated above, there are currently only sparse data concerning the molecular dipoles of the lewisite isomers, including a 1938 study in benzene[4] and a group-additive estimate from 1948.[5] One of the goals of this study was to provide more sophisticated estimates of the dipole moments of the lewisite isomers based on *ab initio* calculations. Table 7 contains the calculated dipole moments of the conformations of the lewisite isomers at a variety of levels of theory.

In general, the calculated dipole moment is reduced upon inclusion of electron correlation. This is a trend that is generally observed for other systems also.[15] Additionally, the dipole moments calculated with the LANL2DZ basis set tend to be larger than those calculated with the all-electron basis sets. For the *geminal* isomer the A conformation possesses the greatest and the C conformation the smallest dipole moment. For the *cis* isomer the C conformation has the higher dipole moment. For the *trans* isomer, the A conformation has the highest dipole moment and the B and C conformations have dipoles of very similar magnitude.

A Boltzmann-weighted averaging of dipole moments based on the conformational energy preferences [using the zero-point energy-corrected MP2/6-311+G(2d,p)//MP2/6–311+G(2d,p) conformational energies] results in average dipole moments for the three lewisite isomers of 2.328 D for the *geminal*, 2.359 D for the *cis* and 2.147 D for the *trans* isomer. These are all larger than the value of 1.77 D obtained in 1938 in benzene.[4] It is useful to compare the data in Table 7 with McDowell *et al.*'s 1948 group-additive estimates of dipole moments.[5] For the *trans* isomer, there is not an individual conformation that has a calculated dipole moment in close agreement with McDowell *et al.*'s value of 2.03 D. However, the Boltzmann-weighted value of 2.328 D is in reasonable agreement. For the *cis* isomer, McDowell *et al.* estimated 2.14 or 3.12 D depending on the degree of free rotation about the C—As bond. These values are in good agreement with the MP2/6–311+G(2d,p)//MP2/6–311+G(2d,p) values in Table 7. The Boltzmann-weighted average value of 2.147 D for the *trans* isomer is also in good agreement with McDowell *et al.*'s estimate of 2.03D.

CONCLUSION

To the best of our knowledge, this work represents the first application of *ab initio* molecular orbital calculations to the study of the isomers of lewisite. Lewisite is an interesting and important system because of its physiological effects, its potential use as a chemical weapon and the challenges associated with its destruction. For all of these reasons the chemical characterization of this system is highly desirable. The application of computational methods to that end is particularly advantageous in the case of lewisite because the difficulty associated with handling this material has made experimental data in the literature somewhat scarce. Specifically, this work was directed at ascertaining the relative stability of the isomers of lewisite, in addition to characterizing the structures, dipole moments and energetic preferences of their conformations.

For the highest levels of theory applied in this study, the *trans* isomer is calculated to be the most stable and the *geminal* isomer is predicted to be the least stable. This is in agreement with the ratios of the isomers that are typically encountered in lewisite preparations. At the highest levels of theory employed, the extended conformation A is calculated to be the most stable for all three lewisite isomers, although the preference for this conformation is very small for the *geminal* isomer.

This study allows a comparison of the results obtained with the LANL2DZ effective core potential basis set and the all-electron 6–311+G(2d,p) and also a comparison of the Hartree–Fock and MP2 levels of theory. Geometries calculated at the HF/LANL2DZ level result in bond lengths that are generally longer (by over 0.1 Å for the As—Cl bonds) than those calculated with the all-electron HF/6–311+G(2d,p) basis set. For either basis set, there are no significant differences in the geometries calculated at the MP2 level as compared with the HF level, although the differences are greater for the LANL2DZ basis set than for 6–311+G(2d,p). A similar trend is seen for conformational energies where the inclusion of electron correlation at the MP2 level also produces more significant changes with LANL2DZ than 6–311+G(2d,p). For the 6–311+G(2d,p) basis set, there are not large differences in conformational energies calculated with MP2 single-point energies at the HF geometry as compared with those obtained from full MP2 optimizations.

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