

Developing a force field for simulation of poly(ethylene oxide) based upon *ab initio* calculations of 1,2-dimethoxyethane

PHILIP M. ANDERSON and MARK R. WILSON*

Department of Chemistry, University of Durham, South Road, Durham, DH1 3LE, UK

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The relative conformational energies in the 1,2-dimethoxyethane (DME) molecule have been extensively studied using B3LYP and MP2 *ab initio* methods, employing a range of commonly used basis sets. These conformational energies have been used to fit new O–C–O and C–O–C–C torsional interaction parameters for the OPLS-AA force field. The resulting force field (DMEFF) shows some improvement in conformational populations, calculated from molecular dynamics simulation of bulk DME, compared to two other commonly used force fields. Extensive reverse-engineering of the OPLS-AA energy function has also allowed the development of additional sets of torsion parameters for these two dihedral types, resulting in a force field that reproduces the conformational behaviour of DME in the liquid phase extremely well.

1. Introduction

1,2-Dimethoxyethane (DME) contains the two major dihedral interactions present in the polymer poly(ethylene oxide) (PEO) (C–O–C–C and O–C–C–O). Consequently, the conformational energies and populations of the former have been extensively studied experimentally [1–6] and theoretically [6–17] in the gas, liquid and aqueous phases to obtain better understanding of the conformational behaviour of the latter.

The conformational behaviour of DME is quite complex. The five conformations which have been found experimentally to dominate the gas and liquid phases of DME are shown in figure 1. DME exhibits a strong *gauche effect*, where the *gauche* conformation of the central O–C–C–O dihedral is unusually highly populated. In fact many X–C–C–Y systems, where X and Y are small electronegative groups, exhibit greater stability in the *gauche* state than *trans* [18], particularly 1,2-difluoroethane [19, 20]. When X and Y are large polarizable groups, the *gauche* state is destabilized with respect to the *trans* state [21].

In 1993, Smith and co-workers performed *ab initio* electronic structure calculations on DME [22] and used the results of these calculations to construct a force field [23] specifically for DME and PEO. This work, however, is now ten years old and, in the past decade, increasingly powerful computers have become more widely available. In particular, although the final energy evaluations were

carried out at the MP2/D95+(2df,p) level, these were carried out with optimized structures obtained at the HF/D95** level. We therefore expect considerable improvements in conformational energies to be possible with a higher level of theory.

In the current work, the DFT and MP2 calculations have been used to optimize the structures of the conformations (*ttt*, *tgt*, *ttg*, *tgg*, *tgg'*, *ggg*, *ggg'*, *gg'g*, *gtg* and *gtg'*) of DME and calculate the energy for several rotational barriers using a variety of basis sets. These optimized energies were then used to parametrize a force field for DME, which was refined by carrying out molecular dynamics calculations of DME in the liquid phase, in an attempt to obtain good agreement with experimental data. An investigation into the nature of the potential energy surface on which the five most populous conformations lie yielded some improvement in the conformational behaviour of simulated liquid DME.

2. Computational

The Gaussian 98 [24] software package was used to optimize the geometries of the ten conformations of DME using MP2 and DFT/B3LYP calculations with a range of common basis sets from STO-3G up to 6-311++G(2d,2p). The two *cis* barriers (*tct* and *ttc*) were also optimized, as were the *tgt–tgg'* and *ttg–tgg'* inter-conformational barriers for some basis sets with MP2. In addition, relaxed potential energy surface scans were carried out at the MP2/6-31++G'(d,p) level of theory with six degree intervals for the *txt*, *ttx* and *tgx* conformations, where *x* is the varying dihedral.

*Author for correspondence.
e-mail: mark.wilson@durham.ac.uk

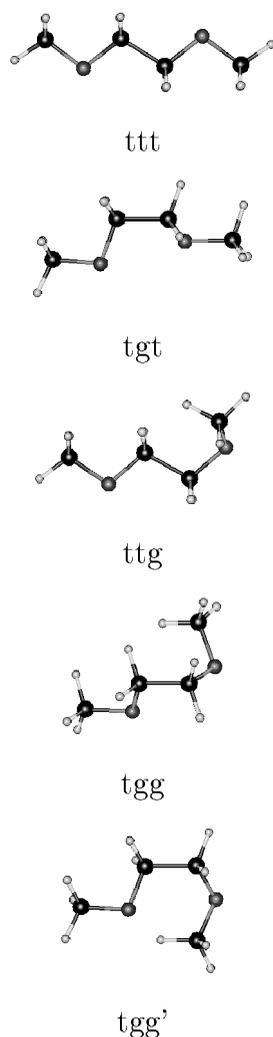


Figure 1. Low energy conformations of DME. The short 1,5-CH-O distance in the tgg' conformation indicates a possible weak internal hydrogen bond.

Torsional force constants were found by a least-squares fit to the *ab initio* potential using the torsional force constants as free parameters. The fitting procedure was as follows:

- (i) start with approximate values for torsional force constants;
- (ii) minimize the energy of the molecule in the force field for each fitted data point;
- (iii) calculate the sum of squared differences between the *ab initio* data and the data obtained from the energy minimizations (equation (1)),

$$\chi^2 = \sum (\Delta E_{i,a} - \Delta E_{i,f})^2, \quad (1)$$

where $\Delta E_{i,a}$ is the *ab initio* energy of conformation i relative to the ground state (lowest energy

- conformation) and $\Delta E_{i,f}$ is the force field energy of conformation i relative to the ground state;
- (iv) carry out a least-squares fitting to minimize χ^2 with respect to changes in the torsional parameters, ensuring that the energy of each fitted data point is re-minimized at each step in the fit.

Although computationally expensive, this process ensures that all other terms in the force field that influence conformational energies are taken into account in the fit. This procedure has previously been used to parametrize a force field for molecules exhibiting liquid-crystalline properties [25].

Once fitted torsion parameters have been obtained, it was necessary to test them in a bulk liquid MD simulation of DME, in order to assess how well the force field reproduced experimentally determined conformational populations. The testing procedure used was the same for all trial force fields and made use of the DLPOLY molecular dynamics simulation code [26]. Periodic boundary conditions were employed with a cubic box geometry. Simulations were carried out in the NpT ensemble at $p = 1$ atm and $T = 300$ K to correspond to the conditions of an earlier Raman spectroscopic study. The starting configuration used was a randomized box of 343 DME molecules; this initial configuration was taken from the end point of a previous equilibrated simulation using the unmodified OPLS-AA force field. The total simulation time was 750 000 time-steps (1 fs time-step, with the first 50 000 steps as equilibration) and a charge-group based cut-off of 7.5 Å was used. The DME molecules in these simulations were split into two neutral charge groups, each comprising exactly half of a DME molecule. Atomic coordinates used to calculate conformational populations were stored once every 500 time-steps. All degrees of freedom within the molecules were left unconstrained. Conformational populations were sampled across a series of time windows in the simulation trajectory data, to ensure that the system had reached equilibrium.

3. Results and discussion

3.1. *Ab initio* structure optimizations of DME

3.1.1. MP2 optimizations

Several *ab initio* relaxed potential energy surface scans were performed on DME, at the MP2/6-31G⁺⁺(d,p) level of theory (figure 2). Comparing the rotational energy profiles of the O-C-C-O (*txt* scan) and C-O-C-C (*ttx* scan) dihedrals reveals a gauche effect at work in the former, where the relative energy of the gauche conformation is significantly lower than in the latter. Results for the single-point MP2 optimized structures are shown in table 1. In some cases, no minimum was found for the $gg'g$ conformation, due

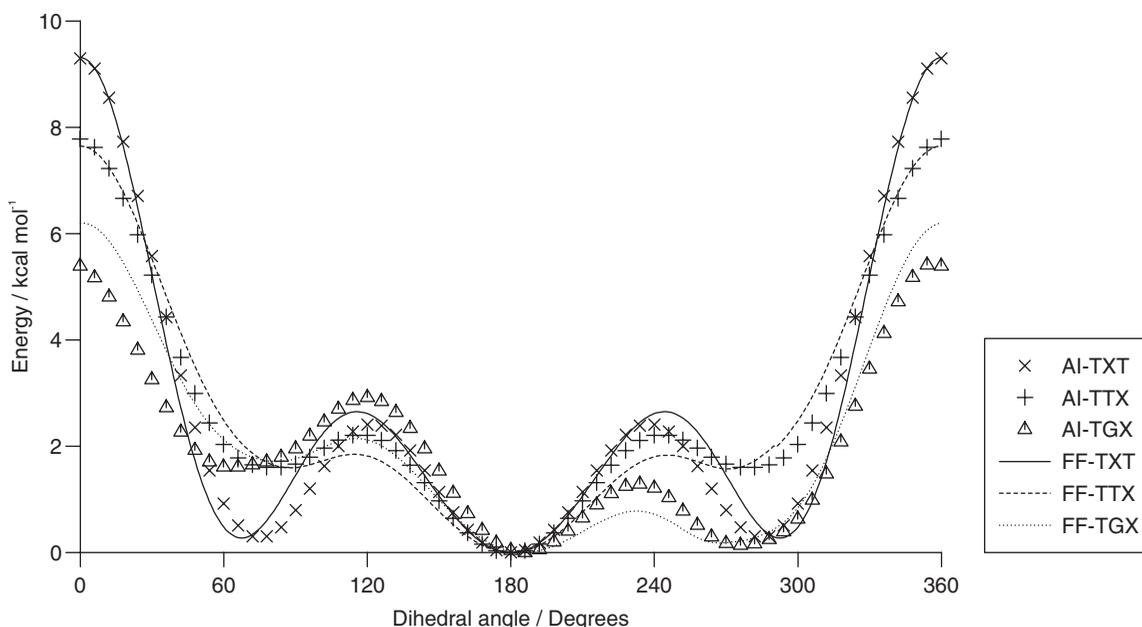


Figure 2. *Ab initio* relaxed potential energy surface scans of DME at the MP2/6-31G'++(d,p) level of theory (AI) and for the DMEFF force field (FF). (The TXT label represents rotation about the central O-C-C-O dihedral, TTX and TGX represent rotation about the terminal C-O-C-C dihedral with the O-C-C-O dihedral in *t* and *g* states respectively.)

Table 1. Optimized energies of various conformations and barriers in DME, using the MP2 method with various basis sets. All energies are in kcal mol⁻¹ and are relative to the lowest energy conformation in each case.

Conformation	STO-3G	3-21G	4-21G	6-31G(d)	6-31++G'(d,p)	6-311++G(d,p)	6-311++G(2d,2p)	D95+(2df,p)
<i>ttt</i>	0.00	1.55	1.54	0.00	0.00	0.00	0.00	0.00 (0.00)
<i>tgt</i>	0.34	3.17	3.09	0.57	0.28	0.19	0.31	0.09 (0.15)
<i>ttg</i>	1.21	2.58	2.57	1.47	1.60	1.51	1.47	1.45 (1.43)
<i>tgg</i>	1.56	4.12	4.06	1.88	1.88	1.72	1.70	1.33 (1.51)
<i>tgg'</i>	0.28	0.00	0.00	0.09	0.42	0.41	0.46	0.12 (0.23)
<i>ggg</i>	2.13	1.87	1.93	1.74	1.80	1.39	1.76	1.29 (1.64)
<i>ggg'</i>	1.54	0.99	1.02	1.60	2.21	2.08	2.02	1.65 (1.86)
<i>gg'g</i>	3.88	2.27	^a	2.07	2.57	2.45	2.32	^a (2.41)
<i>gtg</i>	2.36	3.68	3.65	3.01	3.33	3.23	3.00	3.04 (3.13)
<i>gtg'</i>	2.40	3.29	3.27	2.84	3.22	3.13	2.91	2.93 (3.08)
<i>tct</i>	4.32	11.89	11.73	9.17	9.30	9.20	8.78	8.74 (8.90)
<i>ttc</i>	7.05	8.22	8.30	7.75	7.78	7.73	6.97	7.25
<i>tgt-tgg'</i>					1.50	1.34	1.49	(1.36)
<i>ttg-tgg'</i>					2.92	2.90	2.84	(2.03)

^aNo energy minimum found for this conformation. Values in parentheses are optimized energies at HF geometries from [23].

to the unfavourable close contact between the two terminal methyl groups.

All of the higher-order basis sets give the *ttt* conformation as the global minimum and find the energy gaps to the second and third favoured conformations, *tgt* and *tgg'* respectively, to be very small (<0.5 kcal mol⁻¹). Some convergence of relative energies is seen for most conformations within the 6-31G basis set family. This is particularly the case for the *ttg*, *tgg* and *gtg* conformations. However, the very small energy differences

between conformations means that the percentage changes between basis sets are still quite large. We note that the smaller basis sets (3-21G and 4-21G) give a different order of conformational energies and give the *tgg'* conformation as the preferred structure. MP2 calculations are well known for giving poor results with small basis sets where polarization functions are not included [27-29] and this seems to be the case here.

A set of full optimizations were performed in a previous study by Smith and co-workers [22] using the

HF/D95** level of theory prior to single point energy evaluations at the MP2/D95+(2df,p) level. It is immediately clear that with the exception of *ttg*, all of Smith and co-workers' relative energies are higher than the ones found in this study. This is most likely to be caused by the small strain energy introduced because the optimized structures from the HF calculation do not correspond to energy minima on the MP2/D95+(2df,p) potential energy surface used in their energy evaluation.

Results for the D95+(2df,p) basis set show similar energies for most conformations and barriers. The energies of the *tgt*, *tgg* and *tgg'* conformations are somewhat different from the corresponding energies predicted by other basis sets in the 6-31G family but the general trend is maintained.

Due to current limitations in computational power, higher basis sets (e.g. cc-pVDZ, aug-cc-pVTZ, etc.) and methods (e.g. coupled-cluster) are not easily applicable to such a large system as DME. There are some studies that use focal-point extrapolations [30, 31] to obtain estimates of conformational energies at levels of theory that are too expensive to run on current processors. Such detailed studies may be possible for DME.

3.1.2. B3LYP optimizations

To assess the applicability of density functional theory (DFT) to this system, and to give a basis for comparison with MP2 results, the B3LYP functional was also used in optimizations of the DME molecule for a range of basis sets, as shown in table 2. The B3LYP method appears to have more difficulty in optimizing the *gg'g* conformation than MP2.

The higher basis set B3LYP calculations agree with the earlier MP2 work in predicting the *ttt* conformation as the most stable, followed by *tgt* and *tgg'*. The results

are somewhat more consistent than those in table 1 and, as expected from previous conformational studies of small molecules [29], change less with basis set. The D95+(2df,p) results are also in good agreement with those from the 6-31G family of basis sets. One notable difference is that the DFT results for the *tgg'* conformation are higher, which may indicate that the weak C-H...O internal hydrogen bond (which has been postulated to help stabilize this conformation) may be less well described with B3LYP.

In both the MP2 and B3LYP cases, the 6-31G(d) energy for *tgg'* is significantly lower than the remaining energies in this basis-set family. The *tct* and *ttc* barrier energies are slightly smaller with the B3LYP method than MP2.

3.2. Fitting force field torsion parameters to ab initio data

The commonly used OPLS-AA force field [32, 33], which was designed with the simulation of small, organic molecules in mind, does not perform particularly well in the simulation of liquid DME. Specifically, the conformational populations in bulk liquid DME are in poor agreement with a previous experimental Raman spectroscopic study [4]. A typical MD simulation of liquid DME with the OPLS-AA force field underestimates the quantity of molecules in the *tgg'* conformation, and overestimates the population of the *tgt* conformation (table 3). Similar results are obtained using Smith *et al.*'s DME force field [23].

The energies of the minimized conformations using the OPLS-AA force field also differ quite significantly from the energies obtained using high-level *ab initio* structure optimizations. These facts are sufficient motivation to refit OPLS-AA torsion parameters to

Table 2. Optimized energies of various conformations and barriers in DME, using the DFT/B3LYP method with various basis sets. All energies are in kcal mol⁻¹ and are relative to the lowest energy conformation in each case.

Conformation	STO-3G	3-21G	4-21G	6-31G(d)	6-31++G'(d,p)	6-311++G(d,p)	6-311++G(2d,2p)	D95+(2df,p)
<i>ttt</i>	0.66	1.73	1.73	0.00	0.00	0.00	0.00	0.00
<i>tgt</i>	0.90	3.16	3.09	0.52	0.48	0.46	0.33	0.26
<i>ttg</i>	1.45	2.70	2.70	1.41	1.70	1.63	1.57	1.59
<i>tgg</i>	1.76	4.06	4.02	1.89	2.17	2.11	1.89	1.79
<i>tgg'</i>	0.00	0.00	0.00	0.32	0.81	0.72	0.80	0.70
<i>ggg</i>	2.10	2.16	2.21	2.63	3.04	2.87	2.88	2.71
<i>ggg'</i>	0.93	0.99	1.01	1.86	2.74	2.59	2.58	2.48
<i>gg'g</i>	^a	^a	^a	2.88	^a	^a	3.16	^a
<i>gtg</i>	2.22	3.78	3.75	2.96	3.58	3.45	3.31	3.36
<i>gtg'</i>	2.12	3.38	3.36	2.78	3.35	3.22	3.13	3.18
<i>tct</i>	4.93	11.74	11.60	8.42	8.83	8.90	8.34	8.38
<i>ttc</i>	7.06	8.06	8.16	7.15	7.41	7.39	7.11	7.12

^aNo energy minimum found for this conformation.

Table 3. Conformational populations of DME calculated from molecular dynamics simulations of the bulk liquid for four different force fields.

Conformation	OPLS-				
	AA	Smith ^b	DMEFF	Engineered	Raman ^c
<i>ttt</i>	13.5%	18%	15.4%	13.6%	12%
<i>tgt</i>	50.3%	45%	51.0%	46.6%	42%
<i>ttg</i>	5.2%	9%	5.1%	2.9%	4%
<i>tgg</i>	13.0%	8%	7.8%	4.3%	9%
<i>tgg'</i>	14.6%	17%	18.4%	30.8%	33%
<i>ggg</i>	1.4%	^a	0.4%	0.4%	0
<i>ggg'</i>	1.4%	^a	1.2%	1.0%	0
<i>gg'g</i>	0.1%	^a	0.3%	0.0%	0
<i>gtg</i>	0.3%	^a	0.2%	0.2%	0
<i>gtg'</i>	0.2%	^a	0.2%	0.2%	0

^a Remaining conformations listed as 3%.^b Results from [15].^c Results from [4].

the high-level *ab initio* calculations from section 3.1, in order to obtain a force field that better represents the DME molecule in the gas phase. In turn it is hoped that this good representation will transfer well to the bulk liquid phase and to poly(ethylene oxide) chains in aqueous solution.

Early fit attempts based upon the three-term cosine torsion potential of the OPLS-AA force field gave rise to unreasonably high χ^2 values. Therefore, it was decided to adopt a four-term cosine torsion potential to achieve better fits. Initially, fitting of torsion parameters to the entire rotational energy profile was attempted but was less successful than fitting to unconstrained energy-minimum conformations and barrier peaks. Consequently, the latter has been adopted throughout this paper.

The best fitted force field, denoted DMEFF (fitted torsional parameters shown in table 4 and other data from the Jorgensen OPLS-AA force field given in appendix A), was fitted to the MP2/6-31++G'(d,p) data using the five sets of conformations (*ttt*, *tgt*, *ttg*, *tgg* and *tgg'*) which coexist in the liquid phase of DME. In addition, the major inter-conformational barriers (*tct* and *ttc/ctt*) were also included in the fit (this gives a total of 18 separate conformations). The quality of the fit for the energy-minimum conformations used in the fitting process was quite good ($\chi^2 = 1.16 \times 10^{-5}$ kcal²mol⁻²). Testing for conformations outside the fitted set also gave reasonably good agreement with *ab initio* energy values in almost all cases (as shown in table 5). Only the *ggg* conformation has a poor match for energy in the fitted force field, but since the population of the *ggg* conformation in bulk liquid DME is negligible, this can be overlooked.

Table 4. Torsion parameters for the DMEFF (1) and engineered (2) force fields. (All other force field parameters are taken from the OPLS-AA force field [33]—see appendix A.)

Torsions	$V_1/$ kcal mol ⁻¹	$V_2/$ kcal mol ⁻¹	$V_3/$ kcal mol ⁻¹	$V_4/$ kcal mol ⁻¹
O–C–C–O (1)	2.8198	–2.5606	0.8216	–0.9203
C–O–C–C (1)	1.6678	–0.5653	–0.0033	–0.2931
O–C–C–O (2)	0.7445	–2.9173	2.7935	4.4899
C–O–C–C (2)	–1.5627	2.2732	3.0641	–1.2669

Table 5. Comparison of energies and torsional angles between the fitted force field (DMEFF), the *ab initio* data used in the fit and the engineered force field. ($\phi_1 =$ C–O–C–C–, $\phi_2 =$ –O–C–C–O– and $\phi_3 =$ –C–C–O–C are the three dihedral angles along the DME backbone.)

		Energy/kcal mol ⁻¹	ϕ_1°	ϕ_2°	ϕ_3°
<i>ttt</i>	<i>ab initio</i>	0.00	180	180	180
	DMEFF	0.00	180	180	180
	engineered	0.00	180	180	180
<i>tgt</i>	<i>ab initio</i>	0.28	186	75	186
	DMEFF	0.24	185	68	185
	engineered	0.20	182	80	182
<i>ttg</i>	<i>ab initio</i>	1.60	181	178	81
	DMEFF	1.56	182	175	88
	engineered	1.51	181	179	56
<i>tgg</i>	<i>ab initio</i>	1.88	181	60	63
	DMEFF	1.92	182	63	83
	engineered	1.87	180	77	54
<i>tgg'</i>	<i>ab initio</i>	0.45	182	74	–84
	DMEFF	0.41	184	73	–91
	engineered	–0.46	181	82	–56
<i>gtg</i>	<i>ab initio</i>	3.33	85	179	85
	DMEFF	3.12	85	168	85
	engineered	2.84	55	177	55
<i>gtg'</i>	<i>ab initio</i>	3.22	80	180	–80
	DMEFF	2.89	88	180	–88
	engineered	2.64	56	180	–56
<i>ggg</i>	<i>ab initio</i>	1.80	59	44	59
	DMEFF	3.09	77	55	77
	engineered	2.74	52	73	52
<i>ggg'</i>	<i>ab initio</i>	2.20	78	71	–81
	DMEFF	2.08	83	70	–89
	engineered	1.04	56	80	–55
<i>gg'g</i>	<i>ab initio</i>	2.58	103	–64	103
	DMEFF	1.39	106	–68	106
	engineered	–	–	–	–
<i>tct</i>	<i>ab initio</i>	9.30	180	0	180
	DMEFF	9.31	180	0	180
	engineered	9.21	180	0	180
<i>ttc</i>	<i>ab initio</i>	7.78	180	180	0
	DMEFF	7.68	180	180	0
	engineered	7.48	180	180	0

Despite the good fit obtained above, when these torsion parameters are tested in a molecular dynamics simulation of liquid DME, the resulting conformational populations do not match the measurements taken using Raman spectroscopy, as table 3 shows. The most significant problem in the force field simulations is the low population of the tgg' conformation.

In an attempt to investigate the nature of this problem, a variety of different trial fits were attempted. Fits were attempted to *ab initio* data using higher basis sets without significant improvement in conformational populations in subsequent MD calculations. (Possibly this is because the higher basis sets gave little change in the relative energy of the tgg' conformation, as discussed below. Also, the use of higher basis sets gives a slightly lower tgt energy, relative to the ttt state, and this further increases tgt populations in the liquid phase.) Attempts to weight χ^2 such that lower energy conformations contribute more to this sum than higher energy ones (thereby increasing the formers' significance in the calculation) by using a Boltzmann factor for each conformation in the fit, also failed to give improvements in simulation populations.

The impact of the barrier to rotation in the terminal (hydrogen-bonding end) C–O–C–H dihedral in the tgg' conformation was also investigated without success. Further attempts at improving results by inclusion of extra inter-conformational barriers (particularly the important tgt – tgg' and tgg – tgg' barriers), systematically adjusting the atomic charges (specifically oxygen charges which account for the majority of the electrostatic energy in the overpopulated tgt conformation) and consolidating all torsion potentials into the three fitted dihedrals also failed to have a significant influence on the ratio of tgt and tgg' conformations in the liquid.

Interestingly, artificially increasing the energy of the overpopulated tgt conformation and swapping the energies of the tgg' and tgt conformations failed to have any significant effect on the simulation populations. A significant reduction of the tgg' energy prior to fitting was the only way in which we were able to obtain a force field (denoted 'engineered' force field, parameters in table 4, conformational energies in table 5) with much better agreement between simulation and experiment in the liquid phase. While this is not supported by any of our *ab initio* work, the justification for attempting this comes from the suggestion that the *ab initio* calculations may not be fully taking into account the stabilization energy from the internal hydrogen bond in the tgg' conformation. Interestingly, this force field shows very good agreement with experimental populations (table 3), particularly for the troublesome tgg' conformation. The populations of the tgt and tgg conformations are a little low, but certainly closer

to the Raman populations than tgg' was in previous attempts.

3.2.1. Gas phase behaviour

Table 6 shows results from gas-phase Monte Carlo calculations using standard OPLS-AA and the engineered force field, compared to the two gas-phase experimental studies. It is immediately obvious that the tgg' conformation is much more accessible in this fitted force field, as the MC population has increased to 39% (from 16% in OPLS-AA).

As pointed out by Inomata and Abe [5], the agreement between their NMR study and Astrup's electron diffraction [2] analysis is good for the t/g ratio in the O–C–C–O dihedral but not for the individual conformations themselves. The agreement between the two experiments for the C–O–C–C dihedral is somewhat poorer. As far as the overall t/g population ratios are concerned, the best agreement is seen between the NMR study and the MC calculation using the engineered force field (table 6), but again, there is little agreement between the more highly populated individual conformations. The inconsistency of the different experimental results make further comparisons of gas-phase conformations difficult.

From these results, an oxygen *gauche effect* is obvious; although the C–O–C–C t/g populations remain roughly constant when going from the gas to the liquid phase, the O–C–C–O t/g ratio decreases significantly,

Table 6. Gas phase populations from electron diffraction [2], gas phase NMR [5], MC with standard OPLS-AA force field and MC with engineered force field (fitted to lowered tgg' energy).

Conformation	Diffraction	NMR	OPLS-	
			AA	Engineered
<i>ttt</i>	13%	12%	38.81%	25.92%
<i>tgt</i>	23%	46%	31.64%	30.03%
<i>tgtg</i>	3%	9%	7.71%	2.88%
TGG (<i>tgg</i> + <i>tgg'</i>)	53%	27%	20.13%	40.13%
<i>tgg</i>	–	–	4.01%	1.11%
<i>tgg'</i>	–	–	16.12%	39.02%
GGG (<i>ggg</i> + <i>ggg'</i> + <i>gg'g</i>)	3%	4%	1.28%	0.91%
<i>ggg</i>	–	–	0.39%	0.02%
<i>ggg'</i>	–	–	0.58%	0.89%
<i>gg'g</i>	–	–	0.31%	0.00%
GTG (<i>gtg</i> + <i>gtg'</i>)	5%	2%	0.43%	0.13%
<i>gtg</i>	–	–	0.17%	0.04%
<i>gtg'</i>	–	–	0.26%	0.09%
<i>Trans</i> C–O–C–C	64%	76%	84.37%	77.46%
<i>Gauche</i> C–O–C–C	36%	24%	15.63%	22.54%
<i>Trans</i> O–C–C–O	21%	23%	46.95%	28.93%
<i>Gauche</i> O–C–C–O	79%	77%	53.05%	71.07%

from 23/73 to 16/84. The *gauche* effect is also assisted by the low energy of the O–C–C–O *gauche* state ($\Delta E_{igt-ttt} \approx 0.3 \text{ kcal mol}^{-1}$) compared to the C–O–C–C *gauche* state ($\Delta E_{tgg-ttt} \approx 1.6 \text{ kcal mol}^{-1}$).

Optimizations of hexane at the MP2/6-31G⁺⁺(d,p) level show that the *ttg* and *tgt* conformations are very close in energy, at around $0.6 \text{ kcal mol}^{-1}$, confirming that the oxygens in DME are having a significant effect. Hexane's *tgg'* conformation is unusually high in energy ($2.9 \text{ kcal mol}^{-1}$) compared to its *tgg* energy ($0.9 \text{ kcal mol}^{-1}$). This is due to a close contact between two hydrogen atoms (one on the 1-methyl group and the other in the 5-methylene group), a situation that does not occur in DME due to the absence of the 5-methylene group. The third dihedral (g^-) in hexane has a larger angle than the corresponding DME dihedral because of this extra strain.

3.3 Detailed study of potential energy surface

Despite varying a number of different factors in the fits (most significantly the relative energies of the *tgt* and *tgg'* conformations) the relative populations were not significantly affected, except in the fit of the engineered force field. In order to better visualize the potential energy surface, a Ramachandran map was plotted using the original OPLS-AA force field (figure 3), by varying the O–C–C–O and C–C–O–C dihedrals together, while maintaining the remaining C–O–C–C dihedral in the *trans* state. This map encompasses all five low-energy conformations and the surrounding PES environment.

There are three features immediately noticeable about the *tgg'* sectors on this PES map. First, and most significantly, the *tgg'* potential well is noticeably narrower than the *tgt* well, as noted by Smith *et al.* [23]. This narrow potential well explains why the population of the *tgg'* conformation did not increase significantly, even when the potential well was made slightly deeper (i.e. when the energy of the minimum was reduced slightly in swapping the *tgt* and *tgg'* energies). The depth of the potential has less effect on the accessibility of those states than the width, and only a drastic energy reduction for *tgg'* results in an increased amount of accessible phase space for this conformation.

Second, the large *tgc* energy barrier that lies between the *tgg'* and *tgg* conformations appears to polarize the entire *tgg'* sector towards the *tgt* region. Most notably, the *tgt*–*tgg'* barrier is pushed well into the *tgt* regime. As a result, a particular conformation that may lie on the *tgg'* side of this barrier, and therefore be *tgg'* in spirit, could actually be counted as *tgt*, because it has a C–C–O–C dihedral angle less than 240° . (This is worth considering as it is not possible to accurately determine the exact position of the barriers in the liquid phase.) In fact this is not a significant factor. Modification of the definition of g^+ , t and g^- from the usual ranges of 0° – 120° , 120° – 240° and 240° – 360° to values corresponding to the ranges shown on the Ramachandran map does not have a significant effect on the population results [34].

For the engineered force field, the Ramachandran map (figure 4) shows that the *tgg'* energy well widens

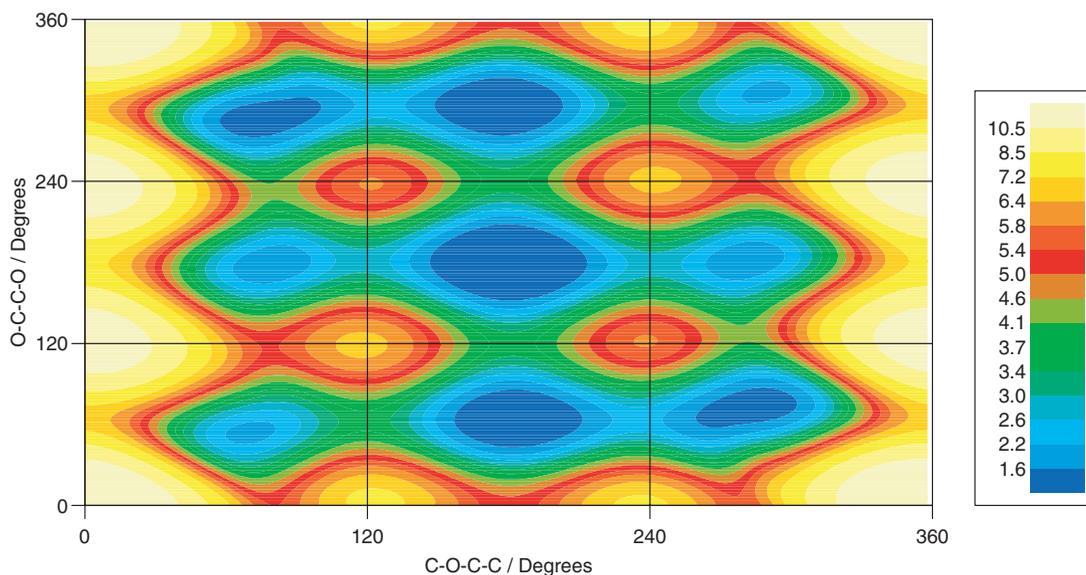


Figure 3. Ramachandran map based upon the O–C–C–O and C–C–O–C dihedrals in DME, using the OPLS-AA force field. The remaining C–O–C–C dihedral is *trans*. All energies are relative to the lowest energy (*ttt*) and are in kcal mol^{-1} . All five low energy conformations are shown: *tgg'* (top left and bottom right), *tgt* (top centre and bottom centre), *tgg* (top right and bottom left), *ttg* (centre left and centre right) and *ttt* (centre).

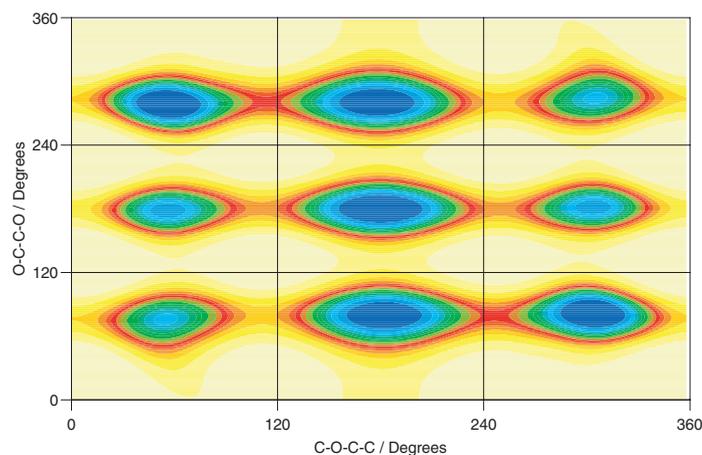


Figure 4. Ramachandran map based upon the O–C–C–O and C–C–O–C dihedrals in DME, using the best force field parameters found in reproducing the *tgg'* population. The remaining C–O–C–C dihedral is *trans*. All energies are relative to the lowest energy (*tgg'*) and are in kcal mol⁻¹. Sector/conformational assignments and colours on the energy scale are as in figure 3.

significantly compared to the DMEFF and the *tgt*–*tgg'* barrier is now biased towards the *tgg'* conformation, increasing the accessibility of this conformation as expected. There is now, however, a more significant biasing of the *tgg'*–*ttg* barrier towards the *ttg* sector, but this does not seem to cause any population problems in simulation. Energy wells for the *ttg* and *tgg* conformations have only been slightly changed, so their populations in the simulation remain in reasonably good agreement with experiment.

4. Conclusions

A detailed set of *ab initio* optimizations have been performed on the DME molecule under the MP2 and B3LYP quantum methods, using a range of basis sets. Two sets of OPLS-AA torsional parameters for the simulation of DME have been fitted to these data. Molecular dynamics simulation in the liquid phase using these force field parameters shows some improvement in conformational populations compared to previous force fields for DME.

There is some evidence from reverse-engineering of the force field that the relatively high *tgg'* population in the liquid phase found in experimental results can only be achieved by a lower relative energy for this conformation than that obtained in this *ab initio* study. As computer power increases it will be interesting to see if higher levels of theory predict a lower energy for this conformation by better representing the stabilization from the weak C–H···O internal hydrogen bond.

It is clear that current force fields such as that of Smith and co-workers and the widely used OPLS-AA are not ideally suited to the simulation of liquid- and gas-phase DME where good conformational agreement

with experiment is required. The narrow potential well of the *tgg'* conformation is responsible for the low population of this conformation predicted using computational methods.

An all-atom force field for DME contains all the terms required for the simulation of the hydrophilic polymer poly(ethylene oxide). In particular the C–O–C–C and the O–C–C–O torsional terms are important in determining the flexibility of a PEO chain. We have recently employed the force field used here to simulate PEO in aqueous solvent and to study the behaviour of PEO grafts in an amphiphilic graft copolymer at the water–air interface [35].

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Appendix A: Additional OPLS-AA force field parameters taken from [32, 33].

Type	q/e^-	$\sigma/\text{\AA}$	$\epsilon/\text{kcal mol}^{-1}$
HC	0.030	2.50	0.030
CT(CH ₂)	0.140	3.50	0.066
CT(CH ₃)	0.110	3.50	0.066
OS	-0.400	2.90	0.140

Bond	$r_0/\text{\AA}$	$k/\text{kcal mol}^{-1} \text{\AA}^{-2}$
CT–CT	1.529	268
CT–HC	1.090	340
CT–OS	1.410	320

Angle	$\theta_0/^\circ$	$k/\text{kcal mol}^{-1} \text{ rad}^{-2}$
CT-CT-HC	110.7	37.5
HC-CT-HC	107.8	33.0
CT-CT-OS	109.5	50.0
OS-CT-HC	109.5	35.0
CT-OS-CT	109.5	60.0

Dihedral	$v_1/\text{kcal mol}^{-1}$	$v_2/\text{kcal mol}^{-1}$	$v_3/\text{kcal mol}^{-1}$
OS-CT-CT-HC	0.0	0.0	0.468
HC-CT-CT-HC	0.0	0.0	0.300
CT-OS-CT-HC	0.0	0.0	0.760

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