

A modification to the COSMIC parameterisation using ab initio constrained potential functions

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SUMMARY

The H..H non-bonded potential employed in the current COSMIC force field has been contrasted with H..H potentials used in a number of other force fields. Initial conversion of the variety of functions to a Morse format, achieved using a simple graphical fitting procedure, allowed a direct comparison to be made, showing the COSMIC potential to differ considerably from the other potentials. This difference was reflected in the failure of COSMIC to reproduce ab initio and experimental energies for molecules with significant H..H interactions, with particular reference to the energy curves of benzophenone and diphenyl ether. Considerable improvement in these energies is produced by the use of a Morse function originally based on the H..H potential used in MM3.

INTRODUCTION

The potential function used in molecular mechanics to describe the van der Waals non-bonded interactions can take one of several forms. A Lennard-Jones 6–12 potential, for example, is used in both the AMBER [1] and CHARMM [2] force fields whereas MM2 [3] uses a function based on the Hill curve. This latter function is also used in the COSMIC force field [4]. Since the Hill potential becomes attractive at close range an alternative term is introduced for short internuclear distances in both MM2 and COSMIC. The term used in the latter force field is shown in Eq. 1.

$$E_{\text{vdW}} = f \cdot (x - y) \quad (1)$$

where $x = 8.28 \cdot 10^5 \cdot \exp[-13.587/P]$, $y = 2.25 \cdot P^6$ ($r_{ij} \geq 1.0 \text{ \AA}$), $y = -2.25/r_{ij}^6$ ($r_{ij} < 1.0 \text{ \AA}$), $P = r_{ij}^*/r_{ij}$, r_{ij} is the distance between atoms i and j and r_{ij}^* is the sum of the vdW radii of i and j .

$$E_{\text{vdW}} = -E_{\text{min}} \cdot (z^2 - 2z) \quad (2)$$

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where $z = \exp[b \cdot (1 - (r_{ij}/r_{\min}))]$, $b = 1n2 \cdot r_{\min}/(r_{\min} - r_0)$, i.e. $r_0 = r_{\min} \cdot (1 - 1n(2)/b)$.

Use of the Morse curve (Eq. 2) as an alternative non-bonded potential has previously been suggested [5] and some examples of its application have appeared in the literature [6, 7]. In contrast to the Hill function, the three variables which define the Morse curve, r_0 , $-E_{\min}$ and r_{\min} (Fig. 1), may be read directly from the curve. In the Hill equation this is true for r_{ij}^* (the sum of the vdW radii and equal to r_{\min}) but not for f (ϵ in MM2), which, as will be shown later, is not equivalent to $-E_{\min}$. The Morse function is thus favoured over the Hill since it is considerably easier, qualitatively, to predict the effect of changing a parameter on the shape of the function, and, furthermore, the simplicity of the Morse variables makes the conversion of other potential functions into a Morse format possible using a simple graphical fitting procedure, described in more detail later. In addition, since the Morse curve remains repulsive at short internuclear distance, adjustments to the function are unnecessary in this region.

Our interest lies in the application of the COSMIC parameterisation to an investigation of energetics in the range of commercially important poly(aryl ether ketone) co-polymers. Thus, calculations have been carried out on relevant small molecules (benzophenone and diphenyl ether) in order to establish, by fitting to ab initio (STO-3G) energies, the most applicable non-bonded potential function. Using a rigid rotor approach (no bond stretching and/or bending terms) with electrostatic and torsional terms (Eqs. 3 and 4, respectively) a series of energies were obtained for each non-bonded potential.

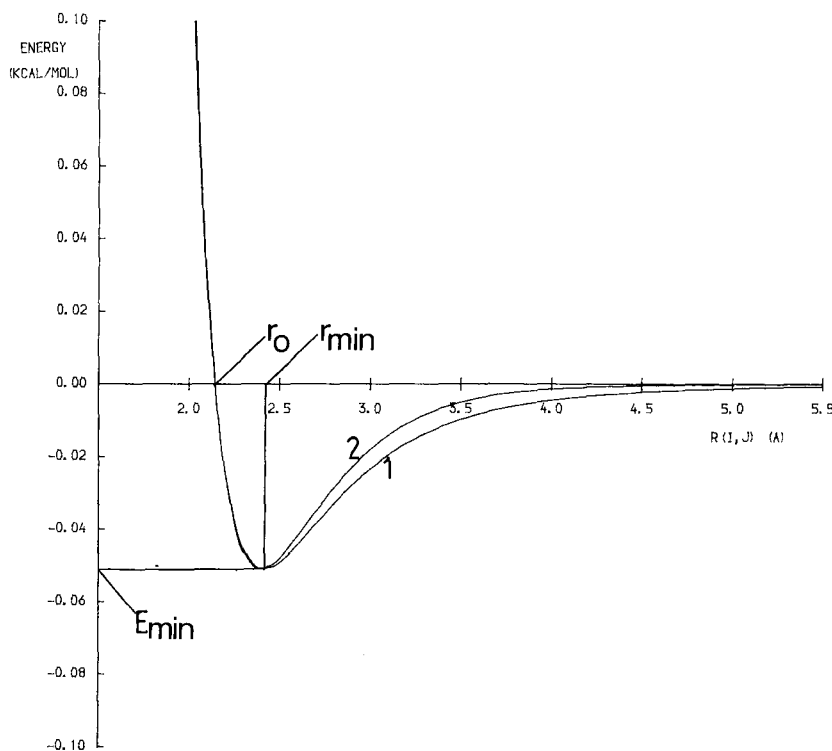


Fig. 1. Parameters used in the Morse curve. Graphical fitting of the Hill function (1) to a Morse function (2).

$$E_{\text{elec}} = 332 * q_i * q_j / r_{ij} \quad (3)$$

where q is the atomic charge.

$$E_{\text{tors}} = V_2 * (1 - \cos 2\theta) / 2 \quad (4)$$

The preferred conformation of the molecules is primarily determined by the large steric interaction between the ortho-hydrogen atoms on opposite rings. This will also be true of the isolated polymer chain; in addition it would be expected that H..H interactions will be predominant when interchain interaction energies are considered. H..H non-bonded potentials have formed the basis of a number of studies [8–10], all of which have concluded that current force fields overestimate the H..H internuclear distance, i.e. the function used becomes too steep in the upper regions of the curve, thus forcing the hydrogen atoms apart in order to relieve the steric energy. In the following study this effect manifests itself in the high energies observed for the planar conformation, since no molecular relaxation is allowed.

COMPUTATIONAL METHOD

(i) *Ab initio* energies

Conformer energy curves for helical ($\theta_1 = \theta_2$, Fig. 2) conformers of benzophenone [11] and diphenyl ether [12] have been obtained using single point STO-3G energies of MNDO-optimised structures. However, comparison of these energies with the available rigid rotor empirical energies is meaningless and therefore further STO-3G calculations were performed using a series of fixed geometry helical conformers, the geometry used being that of the minimum energy conformers from the initial studies. Standard geometries (C–C = 1.40 Å, C–H = 1.08 Å and 120° bond angles) were used for the aromatic rings. The rigid rotor *ab initio* energies thus obtained are particularly exaggerated for near planar conformers but do allow comparison with the empirically generated data.

(ii) *Torsional potentials*

An estimate of the torsional potential around the C–X bond was also obtained from STO-3G energies of MNDO-optimised structures. In order to effectively ‘separate’ the steric and torsional components, θ_1 was maintained at 90° with variation of θ_2 . The extent to which the steric interactions were removed (i.e., kept constant) may be judged by the small variation observed in the MNDO-optimised geometries of the conformers [11, 12]. For benzophenone a simple two-fold

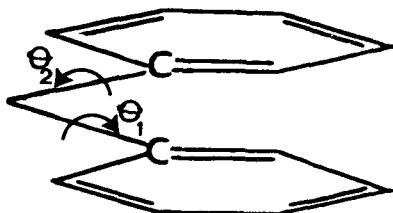


Fig. 2. Definition of θ_1 and θ_2 .

potential was indicated, with $V_2 = 4.8$ kcal/mol. The results for diphenyl ether were inconclusive, possibly due to irregularities in the MNDO optimisation, since, when the calculations were repeated using optimisation at the STO-3G level, the expected two-fold potential ($V_2 = 2.6$ kcal/mol) was indicated. The lower V_2 for diphenyl ether is indicative of the decreased conjugation between the rings and the central function.

(iii) Charges

Atoms are allocated point charges as calculated by the CHARGE2 program [13, 14]. Strictly, charges should be calculated for each conformation, since they are dependent on the extent of the conjugation between rings and central atoms. However, the charges calculated for the planar and $\theta_1 = \theta_2 = 90^\circ$ conformers of benzophenone (the extreme cases) are not significantly different and the calculated energies using the two sets of charges do not differ to any great extent, the maximum error (produced by calculating the energy of the planar conformer using charges calculated for the 90° conformer, or vice versa) being ± 2.8 kcal/mol (the error referring to the difference in energy between the planar and 90° conformers, which is calculated to be 109.3 kcal/mol using the same charges for each conformer). The reduced conjugation in diphenyl ether decreases this error to ± 1.2 kcal/mol, these values being calculated for the selected non-bonded potential (see later). Use of an intermediate conformation to calculate the atomic charges further reduces the error in each case and, since crystal structures of poly(aryl ether) [15] and poly(aryl ether ether ketone) [16] have indicated twist angles of approximately 40° for the aromatic rings, the $\theta_1 = \theta_2 = 40^\circ$ conformer was selected. Charges obtained using this conformer are listed for both molecules in Table 1.

(iv) Derivation of the Morse curve constants

The variables of the Morse functions were obtained from the COSMIC Hill curve by simply reading them from the plotted Hill function for each atom..atom interaction. Since the long-term aim of this work is to apply the Morse function to the entire COSMIC force field, use of a two-parameter Morse was considered desirable. Implementation of this function can then be achieved by simple substitution of the new parameter values into the present COSMIC parameter file. No further adaptations to the COSMIC code, other than changing the function itself, is necessary. R_0

TABLE 1
ATOMIC CHARGES CALCULATED FOR CONFORMERS HAVING $\theta_1 = \theta_2 = 40^\circ$

Atom	Benzophenone	Diphenyl ether
C ₁	-0.040	0.046
C ₂	-0.064	-0.079
C ₃	-0.089	-0.085
C ₄	-0.081	-0.101
H ₁	0.092	0.095
H ₂	0.091	0.091
H ₃	0.091	0.091
C(O)	0.221	-
O	-0.355	-0.162

TABLE 2
HILL AND MORSE PARAMETERS FOR THE H..H NON-BONDED POTENTIAL IN A NUMBER OF FORCE FIELDS

Force field	A ^a	B ^a	ϵ_H	r_{\min}^b	$-E_{\min}$	b	C ^c
COSMIC	8.28	13.59	0.042	2.400	0.051	6.524	0.894
MM2	2.90	12.50	0.047	3.000	0.055	5.776	0.880
Osawa-MM2	2.90	12.50	0.047	2.852	0.055	5.736	0.879
MM3	1.84	12.00	0.020	3.190 ^d	0.022	5.643	0.877

^a A and B are constants in the Hill equation: $E_{vdW} = (\epsilon_1 \epsilon_2)^{0.5} * (-2.25P^6 + A*10^5 * \exp(-B/P))$ where P is defined as in the Introduction.

^b $r_{\min} = 2 * (\text{vdW radius of hydrogen})$.

^c C is a constant given by $C = 1 - (\ln(2)/b)$ and $r_0 = C*r_{\min}$.

^d Modified from the original MM3 value of 3.24 Å, see text.

TABLE 3
-E_{min} VALUES DERIVED FROM THE COSMIC HILL CURVE

Atom	H	C	N	O	F	S	Cl	Br	I
H	0.051	0.081	0.076	0.083	0.082	0.139	0.139	0.164	0.196
C		0.129	0.121	0.134	0.131	0.221	0.221	0.260	0.312
N			0.115	0.127	0.123	0.208	0.208	0.246	0.294
O				0.140	0.135	0.230	0.230	0.271	0.324
F					0.132	0.224	0.224	0.262	0.313
S						0.380	0.380	0.446	0.535
Cl							0.380	0.446	0.535
Br								0.525	0.631
I									0.753

and r_{\min} are related by a parameter, b, known as the steepness parameter (Eq. 2). This latter value was found to be constant for a given Hill function (Table 2), thus allowing r_0 and r_{\min} to be treated as a single variable, i.e. the former being dependent on the latter, reducing the Morse curve to a two-parameter function. Values of $-E_{\min}$ for the COSMIC-derived Morse curve are shown in Table 3, the r_{\min} values are identical to the sum of the COSMIC vdW radii [4]. An example of the graphical fitting used to determine these values is shown (for the H..H interaction) in Fig. 1.

RESULTS AND DISCUSSION

Using the charges and torsional potentials described above, the energies of $\theta_1 = \theta_2$ conformers were calculated for twist angles from 0.0 to 90.0°, the results of which are given in Tables 4 (benzophenone) and 5 (diphenyl ether). The reported energies include an electrostatic contribution, however the same electrostatic term is used for each non-bonded potential function and thus the electrostatic energy is constant for a particular conformer.

TABLE 4
ENERGIES^a CALCULATED FOR HELICAL CONFORMATIONS^b OF BENZOPHENONE USING VARIOUS NON-BONDED POTENTIAL FUNCTIONS AND MNDO/STO-3G CALCULATIONS

$\theta_1 = \theta_2$ (deg)	Energy ^c (kcal/mol)	Energy ^d (kcal/mol)	Energy ^e (kcal/mol)	STO-3G (kcal/mol)
0.0	364.7	293.4	112.5	76.0
10.0	59.0	57.5	39.7	35.7
20.0	2.3	2.5	4.1	7.1
30.0	0.1	0.1	0.0	0.5
40.0	1.4	1.4	1.1	0.6
50.0	3.2	3.2	2.9	1.9
60.0	4.9	4.9	4.6	3.9
70.0	6.4	6.4	6.1	5.4
80.0	7.3	7.3	7.0	6.5
90.0	7.6	7.7	7.4	6.9

^a Quoted values are relative to a low energy conformer of 0.0 kcal/mol using a V_2 value of 4.8 kcal/mol.

^b C-C(O) = 1.515 Å, C=O = 1.230 Å, C-C(O)-C = 121.28°.

^c COSMIC Hill curve.

^d COSMIC-derived two-parameter Morse curve.

^e Morse curve from d including the MM3-derived Morse constants for the H...H non-bonded interaction.

TABLE 5
ENERGIES^a CALCULATED FOR HELICAL CONFORMATIONS^b OF DIPHENYL ETHER USING VARIOUS NON-BONDED POTENTIAL FUNCTIONS AND MNDO/STO-3G CALCULATIONS

$\theta_1 = \theta_2$ (deg)	Energy ^c (kcal/mol)	Energy ^d (kcal/mol)	Energy ^e (kcal/mol)	STO-3G (kcal/mol)
0.0	1253.5	970.3	260.5	173.6
10.0	168.5	142.2	82.0	68.9
20.0	8.1	8.4	10.6	15.2
30.0	0.3	0.3	0.6	2.1
40.0	0.1	0.2	0.1	0.0
50.0	0.9	0.9	0.8	0.6
60.0	1.7	1.7	1.6	1.7
70.0	2.4	2.4	2.4	2.7
80.0	2.9	2.9	2.9	3.4
90.0	3.0	3.0	3.1	3.7

^a Quoted values are relative to a low energy conformer of 0.0 kcal/mol.

^b C-O = 1.376 Å, C-O-C = 121.79°.

^c COSMIC Hill curve.

^d COSMIC-derived two-parameter Morse curve.

^e Morse curve from d including the MM3-derived Morse constants for the H...H non-bonded interaction.

The first series of energies were obtained from the Hill potential taken directly from the COSMIC parameterisation, using the COSMIC f values [4] and a 1.0 Å cutoff term. Reasonable agreement with the *ab initio* energies is seen for conformers with $\theta_1 = \theta_2 > 30^\circ$. There are, however, major discrepancies in empirical energies calculated for the more sterically crowded near-planar conformers, the major contribution to the energy, as might be expected, arising from a large repulsive interaction between the ortho-hydrogens on opposite rings. A second set of energies, calculated using a Morse potential function and COSMIC-derived values of r_{\min} , $-E_{\min}$ (see Table 3) and b (see Table 2) produced similar results. There was a small improvement in the value calculated for the planar conformer, presumably due to the different function shapes in this region caused by the cutoff term used for the Hill curve; the ortho-hydrogen atoms are 0.8 Å (benzophenone) and 0.6 Å (diphenyl ether) apart in this conformation. For all other internuclear distances the two functions are very similar.

Since the major contribution to the excessively high energies obtained above is a large H..H steric interaction, changing the H..H potential whilst maintaining all the remaining values as those derived directly from COSMIC seemed to be a reasonable approach. This was further supported by a series of calculations performed using the original COSMIC force field and full molecular relaxation [12]. These indicated that for molecules such as butane and methyl ethyl ether (in

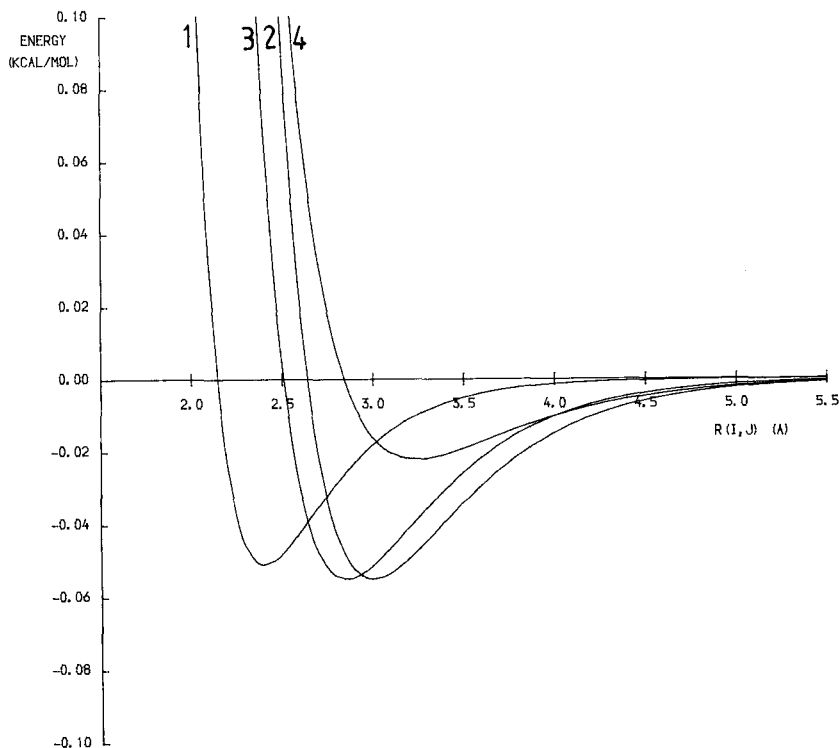


Fig. 3. H..H non-bonded potential functions (Morse format) derived from (1) COSMIC, (2) MM2, (3) Osawa-MM2, (4) MM3. Attractive part of curves.

which H..H interactions are of primary importance) COSMIC did not perform well, with the trans/gauche energy difference being consistently underestimated, compared to experimental values. MM2, in contrast, gave good results with these type of molecules. However, when molecules in which significant H..X interactions occur (e.g. 1,2-dichloroethane, 2,3-dichlorobutane) were considered, the COSMIC energies were in better agreement with experimental data than corresponding MM2 values.

Consideration of the above results allowed a qualitative assessment of the required change in the shape of the H..H potential. The benzophenone/diphenyl ether study indicates that a softer H..H interaction is required at close range (less than r_0). The over-stabilisation of the gauche-butane suggests that the function is too attractive at interatomic distances approximately equal to r_{\min} . Thus the desired function will be one that is displaced to higher energy and 'tipped' to the left. This could have been achieved by arbitrarily changing the r_{\min} and $-E_{\min}$ values. However, as an alternative, several other Morse functions were derived from H..H potentials used in published force fields (see Table 2), using a similar graphical fitting procedure to that described earlier. Thus potentials (Figs. 3 and 4) derived from MM2, Osawa-MM2 (a modified version of MM2 in which a primary target was the improvement of the H..H potential) [8] and the recently

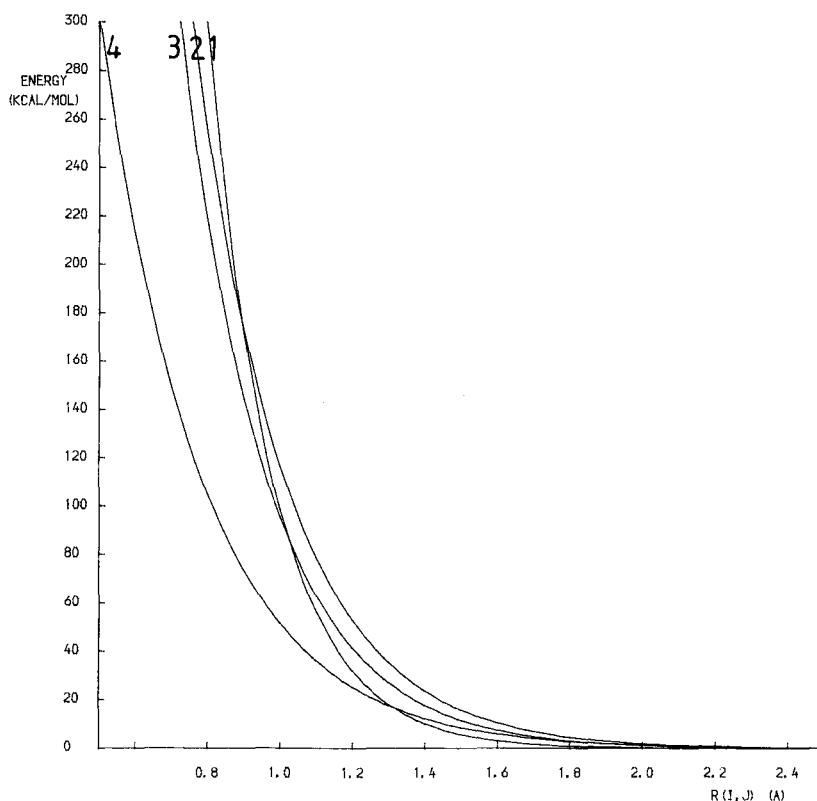


Fig. 4. H..H non-bonded potential functions (Morse format) derived from (1) COSMIC, (2) MM2, (3) Osawa-MM2, (4) MM3. Repulsive part of curves.

published MM3 [10] were used in a further series of rigid rotor calculations. All other interactions were based on the COSMIC-derived Morse parameters. The MM3 function appeared to have the most suitable shape and the energies produced (see Tables 2 and 3) were in good agreement with the ab initio energies, with considerable improvement in the energy of the planar conformer. Furthermore, the optimum twist angles indicated for benzophenone (30°) and diphenyl ether (36°) agree extremely well with experimentally determined values (see Ref. 17 for a review). Calculations using MM2- and Osawa-MM2-derived Morse functions also produced some improvement in the empirical energies but not to the same extent as the MM3-modified potential. It should be noted that the H..H r_{\min} value used in the latter case (3.19 \AA) differs slightly from the MM3 value (3.24 \AA). Whilst this change produces no significant effect on the benzophenone and diphenyl ether energies a more rigorous study of the H..H and other non-bonded potentials currently being undertaken [18] does show this adjustment to be necessary. We believe the small change to be a reflection of the simpler treatment of the C–H bond in COSMIC. In MM3 the interatomic distance used in the non-bonded energy calculation is not calculated from the H atomic centre but rather from a position offset a small distance along the C–H bond. In COSMIC all non-bonded energies are calculated using interatomic distances based on atomic centres.

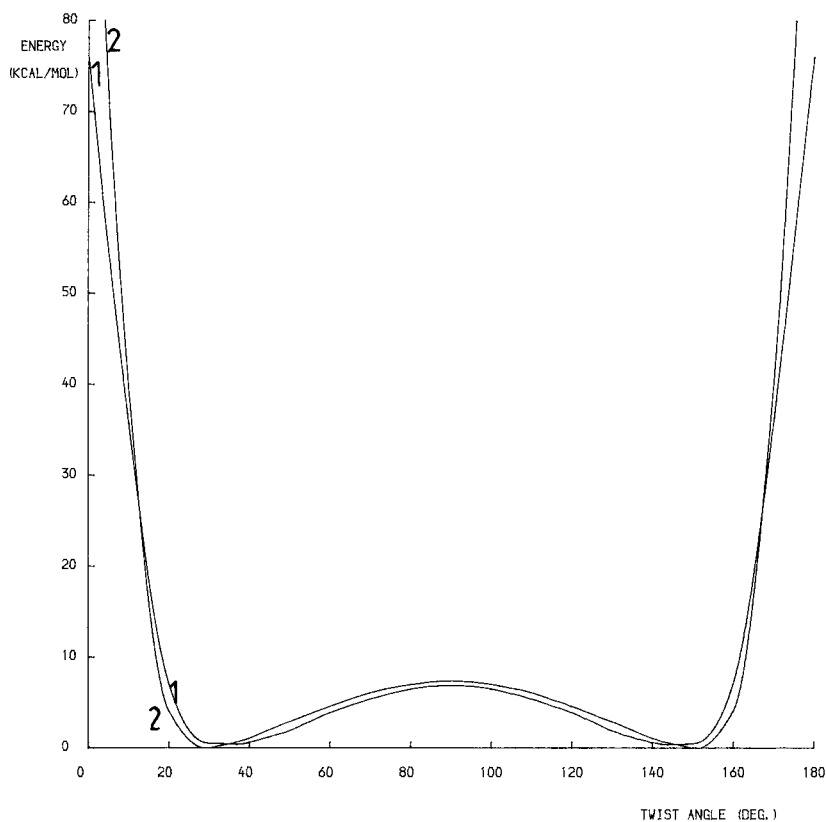


Fig. 5. Energy curves for benzophenone: (1) STO-3G and (2) MM3-modified, COSMIC-derived Morse potential.

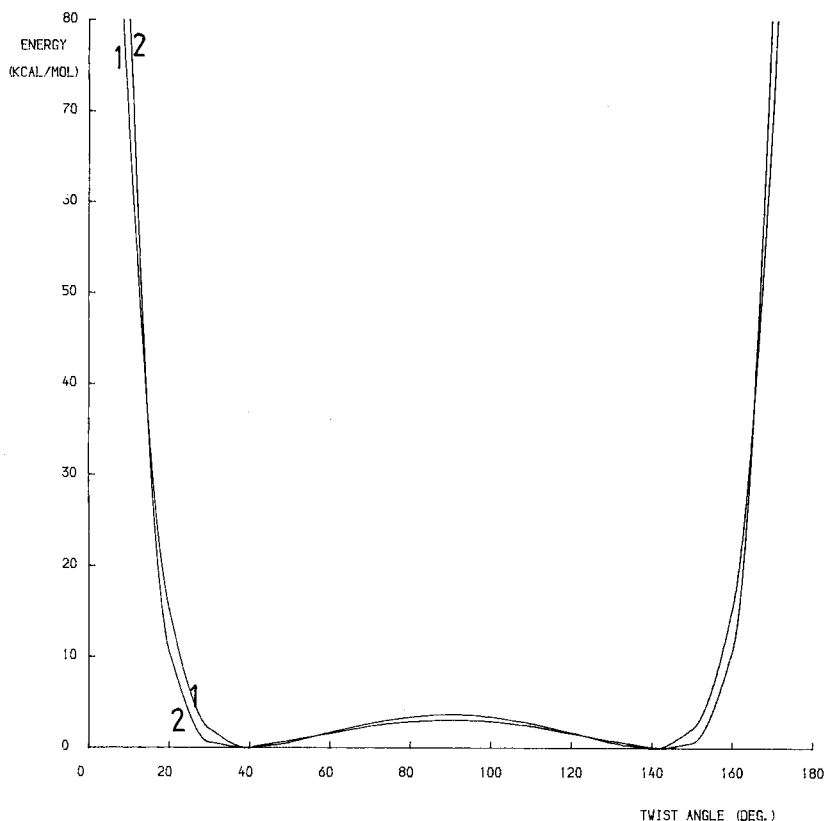


Fig. 6. Energy curves for diphenyl ether: (1) STO-3G and (2) MM3-modified, COSMIC-derived Morse potential.

Rigid rotor energy curves calculated using the COSMIC-derived Morse function with the MM3 H..H modification are shown in Figs. 5 (benzophenone) and 6 (diphenyl ether) together with the corresponding STO-3G energy curve. With the exception of the high-energy, near-planar conformers, agreement between theoretical and empirical energies is good with the rotational barrier via the $\theta_1 = \theta_2 = 90^\circ$ form being adequately reproduced for each molecule. The theoretical and empirical minimum energy conformers are, in each case, slightly different, however, this is because the STO-3G energies indicate, for both molecules, a twist angle a few degrees higher than that found experimentally [17].

CONCLUSIONS

Calculations performed using the original COSMIC constants and the Hill potential function have indicated that there is considerable scope for improvement of these values. A full parameterisation has not been attempted, however it has been shown that an adjustment of the H..H potential function alone can have a significant effect on the correlation of the empirical energies with experimental values. The initial conversion of the Hill function to a Morse curve (for each type of

interaction) essentially produced no change in the calculated energies, an important observation since, if this change is applied to the full COSMIC force field, the non-bonded potential function will remain compatible with the other constants (stretching, bending, torsional, etc.). Simple substitution of the MM3 H..H potential (in Morse format) for the COSMIC H..H function considerably improved the agreement of the empirical energies with rigid rotor STO-3G energies and predicted minimum energy conformers in good agreement with experimental studies. It is acknowledged that as the present work is limited, both in the range of compounds studied and in the restricted approach to the variation of bond lengths and bond angles, no firm conclusions can be drawn until the new non-bonded potentials have been examined utilising the entire force field for a number of compounds. However, the limited objective of reproducing the benzophenone and diphenyl ether STO-3G energy curves is achieved by the modified parameters, providing a reasonable H..H potential which can now be used as a starting point in the development of further non-bonded potentials.

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REFERENCES

- 1 Weiner, P.K. and Kollman, P.A., *J. Comp. Chem.*, 2 (1981) 287–303.
- 2 Brooks, B.R., Bruccoleri, R.E., Olafson, B.D., States, D.J., Swaminathan, S. and Karplus, M., *J. Comp. Chem.*, 4 (1983) 187–217.
- 3 Allinger, N.L., *J. Am. Chem. Soc.*, 99 (1977) 8127–8134.
- 4 Vinter, J.G., Davis, A. and Saunders, M.R., *J. Comput.-Aided Mol. Design*, 1 (1987) 31–51.
- 5 Abraham, R.J. and Stolevik, R., *Chem. Phys. Lett.*, 58 (1978) 622–624.
- 6 Abraham, R.J. and Stolevik, R., *Chem. Phys. Lett.*, 77 (1981) 181–185.
- 7 Stolevik, R. and Thingstad, O., *J. Mol. Struct. Theochem.*, 106 (1984) 333–353.
- 8 Jaime, C. and Osawa, E., *Tetrahedron*, 39 (1983) 2769–2778.
- 9 Ermer, O. and Mason, S.A., *J. Chem. Soc., Chem. Commun.*, (1983) 53–54.
- 10 Allinger, N.L. and Lii, J.H., *J. Comp. Chem.*, 8 (1987) 1146–1153.
- 11 Abraham, R.J. and Haworth, I.S., *J. Chem. Soc., Perkin Trans. 2*, in press.
- 12 Abraham, R.J. and Haworth, I.S., unpublished results.
- 13 Abraham, R.J. and Smith, P.E., *J. Comp. Chem.*, 9 (1988) 288–297.
- 14 Abraham, R.J. and Grant, G.H., *J. Comp. Chem.*, 9 (1988) 244–256.
- 15 Boon, J. and Magre, E.P., *Makromol. Chem.*, 126 (1969) 130–138.
- 16 Fratini, A.V., Cross, E.M., Whitaker, R.B. and Adams, W.W., *Polymer*, 27 (1986) 861–865.
- 17 Baraldi, I., Gallinella, E. and Momicchioli, F., *J. Chim. Phys.*, 83 (1986) 655–664.
- 18 Abraham, R.J. and Haworth, I.S., manuscript in preparation.