Theoretical Studies of Trans-Alkene Mycolic Acid

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Abstract

Theoretical studies carried on *trans*-alkene mycolic acid (MA) that characterize (2*R*,3*R*,17*R*,39*S*,40*S*,*E*)-3-hydroxy-39-methoxy-17,40-dimethyl-2-*tetra* cosyl- octapentacont-18-enoic acid (1). The stereochemistry of MA was showed that the chiral centres in C(19), C(20), C(44), C(49) and C(51) were in (*S*), (*S*), (*R*), (*R*) and (*R*) configurations respectively and the double bond in C(42)-C(43) was described as *E*-isomer. The results of conformational energy for selected (85) conformers in the acid structure were showed that the torsion angles (ψ) were in the range (±180) and this indicate the folding of MA a way same to that present in biomolecules. Theoretical studies of torsional strain (E) of each conformer were showed that the MA has eclipsed and staggered conformation. Internal coordinate mechanics (ICM) of MA was showed that the angle type in most of atoms was dihedral. The bond lengths, bond angles, torsion angles and dihedral angles were also studied, in order to study their effect in the molecule properties and their consequence in the molecular mechanics (MM2) and optimal minimization. Thus, the MM2 properties were envisioned, the results were showed that the torsion energy and the total energy were equal to 13.3334 and 255.0187 kcal/mol respectively. High Van der Waals (VDW) interactions of this MA were observed, due to the dipole/ dipole was not computed. Further, the results of MM2 minimization for MA were showed that the torsion energy and the total energy were equal to 8.8418 and 62.9851 kcal/mol respectively. Thus, the dipole/ dipole (0.2185) of acid was detected after minimization. The results after minimization were showed a significant increase in the actual close contact of atoms. Also, the results were displayed that the carboxylic O(47) atom was close contact with H(179) atom that bonded with alkane C(49) atom in mycolic motif. Further, the molecular mechanics force field (MMFF94) energy and gradient for MA were also calculated. The results were showed that the total energy and RMS gradients were equal to 228.561 kcal/mol and 17.735 respectively. The final energy of MMFF94 minimization and minimization/ sampling were equal to 11.2963 kcal/mol and 11.1221 kcal/mol respectively, which indicated that the minimization was attended successfully.

Keywords: *Mycobacterium tuberculosis*, Mycolic acid, Internal coordinates

1. Introduction

Mycolic acids (MAs) are structural components of the mycobacterial cell wall that have been implicated in the pathogenicity and drug resistance of certain mycobacterial species.1 They also offer potential in area such as rapid serodiagnosis of human and animal tuberculosis. Routes to single enantiomers of hydroxy, methoxy and keto MAs containing an α-methyl-*trans*-alkene unit as well as related trehalose, glucose, arabinose and glycerol esters are described in serodiagnostic assays to detect antibodies to mycobacterial lipids.2 It is increasingly recognized that the conformational behavior of MAs is very important in understanding all aspects of their function. Atomistic molecular dynamics simulations, in vacuo, of stereochemically defined *mycobacterium tuberculosis* MAs show that they fold spontaneously into reproducible conformational groupings. One of the three characteristic mycolate types, the keto-MAs, behaves very differently from either α-MAs or methoxy-MAs, suggesting a distinct biological role.1 However, subtle conformational behavioral differences between all the three MAs types were indicated that cooperative interplay of individual MAs may be important in the biophysical properties of the mycobacterial cell envelope and therefore in pathogenicity.1

Internal coordinates are an attractive alternative to the Cartesian coordinates of each atom when particular degrees of freedom are not of interest.3 Internal coordinates such as bond lengths, bond angles, and torsion angles are natural coordinates for describing a bonded molecular system.4 It has recently been suggested by Mu *et al*. [Proteins 58, 45 2005)] to use backbone dihedral angles instead of Cartesian coordinates in a principal component analysis of molecular dynamics simulations. Dihedral angles may be advantageous because internal coordinates naturally provide a correct separation of internal and overall motion, which was found to be essential for the construction and interpretation of the free energy landscape of a biomolecule undergoing large structural rearrangements.5 which describe the essential physics of a biomolecular process such as protein folding or molecular recognition.3 Molecular modeling can be considered as a range of computerized techniques based on theoretical chemistry methods and experimental data that can be used either to analyse molecules and molecular systems or to predict molecular, chemical, and biochemical properties.6

One of the major advantages of MM2 compared to other computational techniques is the relative ease with which structures can be optimized via minimization of the corresponding potential energy functions.7 The area of MM2 is to study the detailed structure and physical properties of molecules.8

Thomas,9 introduced MMFF94, the initial published version of the Merck molecular force field

(MMFF). It describes the objectives set for MMFF, the form it takes, and the range of systems to which it applies. This study also outlines the methodology employed in parameterizing MMFF94 and summarizes its performance in reproducing computational and experimental data.9

2. Result and discussion

The *trans*-alkene MA.2 that characterize (2*R*,3*R*,17*R*,39*S*,40*S*,*E*)-3-hydroxy -39-methoxy-17,40 –dimethyl-2-tetracosyl-octapentacont-18-enoic acid (1) was studied theoretically, see Figure (1) below. Elemental analysis results of MA were showed that the C, 81.40; H, 13.50 and O, 5.10, but the abundance was equal to 38.04%. Thus, the stereochemistry was also calculated, the results were displayed that the chiral centers in C(19), C(20), C(44), C(49) and C(51) were in (*S*), (*S*), (*R*), (*R*) and (*R*) configurations respectively, but the double bond in C(42)-C(43) was described as *E*-isomer.
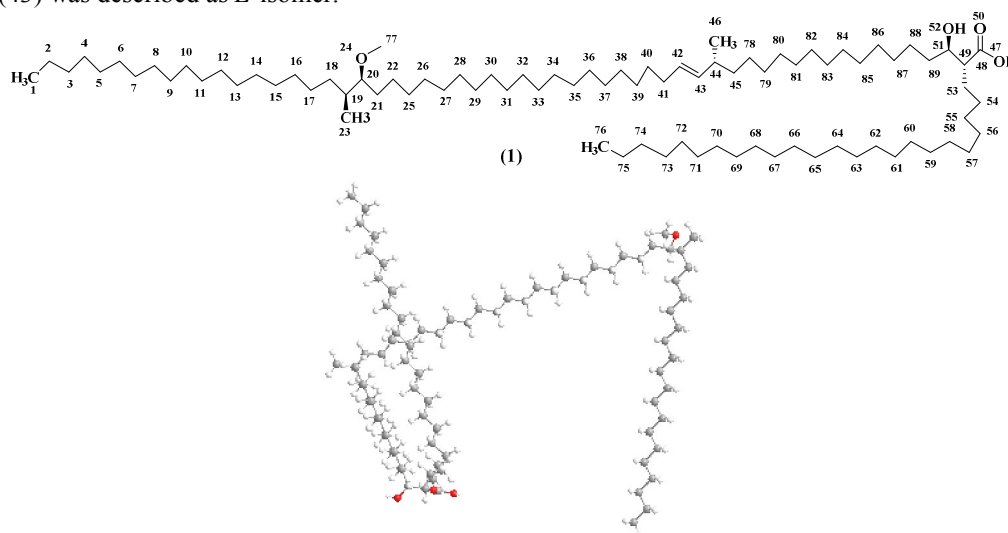

Figure 1. The structure of *trans*-alkene MA (1)

The bonds length between atoms were also intended hypothetically, the results were showed that the actual and optimal bonds length of most of C-C were equal to 1.523 Å in each and the actual and optimal bonds length of most of C-H were equal to 1.113 Å in each. But, the results were indicated high difference between actual and optimal bonds length in other selected C-C, C-H, C-O, O-H and C=O bonds as seen in table (1) below.

Table 1: The selected bond length of atoms in MA (1)

No	Atoms	Bond Length Å	
		Actual Å	Optimal Å
1	C(77)-H(232)	1.113	1.111
2	C(77)-H(231)	1.113	1.111
3	O(52)-H(181)	0.942	0.961
4	C(51)-H(180)	1.113	1.111
5	C(51)-C(89)	1.523	1.514
6	C(51)-O(52)	1.402	1.401
7	C(49)-C(51)	1.523	1.514
8	C(48)-O(50)	1.208	1.208
9	C(48)-C(49)	1.509	1.509
10	O(47)-H(178)	0.972	0.972
11	O(47)-C(48)	1.338	1.338
12	C(43)-H(171)	1.100	1.100
13	C(43)-C(44)	1.497	1.497
14	C(42)-H(170)	1.100	1.100
15	C(42)-C(43)	1.337	1.337
16	C(41)-C(42)	1.497	1.497
17	O(24)-C(77)	1.402	1.396
18	C(20)-H(128)	1.113	1.111
19	C(20)-O(24)	1.402	1.382
20	C(20)-C(21)	1.523	1.514
21	C(19)-C(20)	1.523	1.514

The table shows significant difference between actual and optimal bonds length of alcohol O(52)-H(181) which equal to 0.942 Å and 0.961 Å respectively. Though, the actual and optimal bonds length of carboxylic O(47)-C(48) were equal to 1.338 Å in each, but the actual and optimal bonds length of carboxylic O(47)- H(178) were equal to 0.972 Å in each. Thus, the actual and optimal bonds length of carbonyl C(48)-O(50) were equal to 1.208 Å in each. The actual and optimal bonds length of ether C(20)-O(24) were equal to 1.402 Å

and 1.382 Å respectively. Further, the actual and optimal bonds length of C=C were equal to 1.337 Å in each.

A straightforward method for predicting the protein structure is to find conformations that have the lowest energy along a chosen folding pathway.10 One approach in this direction is to produce a large number of structures by varying the dihedral angles of the molecule more or less randomly and then to screen each one using a suitable energy function.10 Thus, the dihedral angles for MA (1) were calculated as seen in table (2) below.

Table 2. The dihedral angles for selected atoms in MA (1)

No	Atoms	Dihedral angle
1	C(87)-C(88)-C(89)-C(51)	180
10	C(86)-C(87)-C(88)-C(89)	180
19	C(85)-C(86)-C(87)-C(88)	179.999
37	C(83)-C(84)-C(85)-C(86)	-179.999
46	C(82)-C(83)-C(84)-C(85)	-180
55	C(81)-C(82)-C(83)-C(84)	180
64	C(80)-C(81)-C(82)-C(83)	180
73	C(79)-C(80)-C(81)-C(82)	-180
82	C(78)-C(79)-C(80)-C(81)	-180
91	C(45)-C(78)-C(79)-C(80)	180
109	C(73)-C(74)-C(75)-C(76)	-180
118	C(72)-C(73)-C(74)-C(75)	-179.999
127	C(71)-C(72)-C(73)-C(74)	180
136	C(70)-C(71)-C(72)-C(73)	180
145	C(69)-C(70)-C(71)-C(72)	180
154	C(68)-C(69)-C(70)-C(71)	-180
163	C(67)-C(68)-C(69)-C(70)	-180
172	C(66)-C(67)-C(68)-C(69)	-180
181	C(65)-C(66)-C(67)-C(68)	180
190	C(64)-C(65)-C(66)-C(67)	-180
199	C(63)-C(64)-C(65)-C(66)	-180
208	C(62)-C(63)-C(64)-C(65)	180
217	C(61)-C(62)-C(63)-C(64)	-180
226	C(60)-C(61)-C(62)-C(63)	180
235	C(59)-C(60)-C(61)-C(62)	179.999
244	C(58)-C(59)-C(60)-C(61)	180
253	C(57)-C(58)-C(59)-C(60)	-180
262	C(56)-C(57)-C(58)-C(59)	-180
271	C(55)-C(56)-C(57)-C(58)	-60
280	C(54)-C(55)-C(56)-C(57)	180
289	C(53)-C(54)-C(55)-C(56)	180
298	C(49)-C(53)-C(54)-C(55)	-180
307	C(49)-C(51)-C(89)-C(88)	60
310	O(52)-C(51)-C(89)-C(88)	-59.961
319	C(48)-C(49)-C(53)-C(54)	119.999
322	C(51)-C(49)-C(53)-C(54)	-120.001
332	C(53)-C(49)-C(51)-C(89)	0.038
337	O(47)-C(48)-C(49)-C(51)	-180
338	O(47)-C(48)-C(49)-C(53)	-60.035
341	O(50)-C(48)-C(49)-C(53)	119.964
345	C(44)-C(45)-C(78)-C(79)	180
363	C(43)-C(44)-C(45)-C(78)	-120
366	C(46)-C(44)-C(45)-C(78)	120.036
372	C(42)-C(43)-C(44)-C(45)	60
373	C(42)-C(43)-C(44)-C(46)	179.964
378	C(41)-C(42)-C(43)-C(44)	180
382	C(40)-C(41)-C(42)-C(43)	-180
388	C(39)-C(40)-C(41)-C(42)	-180
397	C(38)-C(39)-C(40)-C(41)	-180
406	C(37)-C(38)-C(39)-C(40)	180
415	C(36)-C(37)-C(38)-C(39)	180
424	C(35)-C(36)-C(37)-C(38)	-180
433	C(34)-C(35)-C(36)-C(37)	-180
442	C(33)-C(34)-C(35)-C(36)	179.999
451	C(32)-C(33)-C(34)-C(35)	-180
460	C(31)-C(32)-C(33)-C(34)	-179.999
469	C(30)-C(31)-C(32)-C(33)	180
478	C(29)-C(30)-C(31)-C(32)	179.999
487	C(28)-C(29)-C(30)-C(31)	-180
496	C(27)-C(28)-C(29)-C(30)	-180
505	C(26)-C(27)-C(28)-C(29)	180

No	Atoms	Dihedral angle
514	C(25)-C(26)-C(27)-C(28)	-180
523	C(22)-C(25)-C(26)-C(27)	-180
535	C(21)-C(22)-C(25)-C(26)	180
544	C(20)-C(21)-C(22)-C(25)	180
553	C(19)-C(20)-O(24)-C(77)	-179.996
554	C(21)-C(20)-O(24)-C(77)	60.005
556	C(19)-C(20)-C(21)-C(22)	120.001
559	O(24)-C(20)-C(21)-C(22)	-120.037
574	C(18)-C(19)-C(20)-C(21)	-119.998
575	C(18)-C(19)-C(20)-O(24)	120.04
577	C(23)-C(19)-C(20)-C(21)	120.035
578	C(23)-C(19)-C(20)-O(24)	0.073
583	C(17)-C(18)-C(19)-C(20)	59.999
584	C(17)-C(18)-C(19)-C(23)	179.964
592	C(16)-C(17)-C(18)-C(19)	180
601	C(15)-C(16)-C(17)-C(18)	180
610	C(14)-C(15)-C(16)-C(17)	180
619	C(13)-C(14)-C(15)-C(16)	180
628	C(12)-C(13)-C(14)-C(15)	180
637	C(11)-C(12)-C(13)-C(14)	180
646	C(10)-C(11)-C(12)-C(13)	180
655	C(9)-C(10)-C(11)-C(12)	180
664	C(8)-C(9)-C(10)-C(11)	180
682	C(6)-C(7)-C(8)-C(9)	180
691	C(5)-C(6)-C(7)-C(8)	180
700	C(4)-C(5)-C(6)-C(7)	180
709	C(3)-C(4)-C(5)-C(6)	180
718	C(2)-C(3)-C(4)-C(5)	180
727	C(1)-C(2)-C(3)-C(4)	180

Dihedral angles $\varphi \in [0°, 360°]$ represent circular (or directional) data.5 Unlike the case of regular data $x \in [-\infty, \infty]$, the definition of a metric is not straightforward, which makes it difficult to calculate distances or means. For example, the regular data $x_1=10$ and $x_2=350$ clearly give $\Delta x = |x_2-x_1| = 340$ and $\langle x \rangle = (10 + 350)/2 = 180$. A visual inspection of the corresponding angles $\varphi_1 = 10°$ and $\varphi_2 = 350°$, on the other hand, readily shows that $\Delta x = 20° \neq |\varphi_2-\varphi_1|$ and $\langle \varphi \rangle = 0° \neq |\varphi_2-\varphi_1|/2$. To recover the standard rules of calculating distances and the mean, they assume that $\varphi \in [-180°, 180°]$. Then $\varphi_1 = 10°$ and $\varphi_2 = -10°$, and they obtain $\Delta \varphi = |\varphi_2-\varphi_1| = 20°$ and $\langle \varphi \rangle = (\varphi_2-\varphi_1)/2 = 0°$.5 This example manifests the general property that, if the range of angles covered by the data set is smaller than 180°, this may simply shift the origin of the angle coordinates to the middle of this range and perform standard statistics. The situation is more involved for "true" circular data whose range exceeds 180°.5 This is the case for folding biomolecules, since the ψ angle of the peptide backbone is typically distributed as $\psi_\alpha \approx -60° \pm 30°$ (for αR helical conformations) and $\psi_\beta \approx 140° \pm 30°$ (for β extended conformations). This represents the circular statistics' equivalent of the normal distribution for regular data. However, this method is not applicable to the description of conformational transitions, since the corresponding dihedral angle distributions can only be typically described by multi peaked probability densities.5 Thus, the conformational energy for 85 conformers in MA (1) was studied theoretically. The results were displays that the E of each conformer in MA was had eclipsed and staggered conformation depend on high and low energy respectively. For example the conformer (1) H(179)-O(47)-C(48)-O(50) as seen in Figure (2) below was showed that the E(-100°) and E(100°) which equal to 263.53 kcal/mole and 263.76 kcal/mole respectively, were have eclipsed conformers, but the E(-180°), E(0°) and E(-180°) which equal to 259.18, 255.01 kcal/mole and 259.18 kcal/mole respectively, were have staggered conformers.
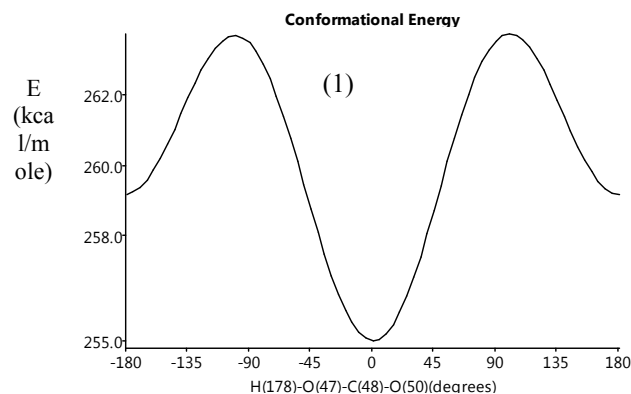
Figure 2. The conformational energies in MA (1)

The results were showed that the ψ angles of MA (1) were in the range (±180) and this can showed that the MA can folding in a way same to that present in biomolecules. However, the ICM using a combination of theoretical data for MA (1) was attended as seen in table (3) below.

Table 3. Internal coordinate mechanics (ICM) of MA (1)

No	Atom	Bond Atom	Bond Length (Å)	Angle Atom	Angle (°)	2nd Angle Atom	2nd Angle (°)	2nd Angle Type
1	C(42)							
2	C(43)	C(42)	1.337					
3	C(41)	C(42)	1.497	C(43)	120			
4	H(170)	C(42)	1.1	C(41)	120	C(43)	120	Pro-S
5	C(44)	C(43)	1.497	C(42)	120	C(41)	180	Dihedral
6	H(171)	C(43)	1.1	C(42)	120	C(44)	120	Pro-S
7	C(40)	C(41)	1.523	C(42)	109.5	C(43)	-180	Dihedral
8	H(168)	C(41)	1.113	C(40)	109.442	C(42)	109.442	Pro-S
9	H(169)	C(41)	1.113	C(40)	109.462	C(42)	109.462	Pro-R
10	C(39)	C(40)	1.523	C(41)	109.5	C(42)	-180	Dihedral
11	H(166)	C(40)	1.113	C(39)	109.441	C(41)	109.442	Pro-S
12	H(167)	C(40)	1.113	C(39)	109.461	C(41)	109.462	Pro-R
13	C(38)	C(39)	1.523	C(40)	109.5	C(41)	-180	Dihedral
14	H(164)	C(39)	1.113	C(38)	109.442	C(40)	109.442	Pro-S
15	H(165)	C(39)	1.113	C(38)	109.462	C(40)	109.461	Pro-R
16	C(37)	C(38)	1.523	C(39)	109.5	C(40)	180	Dihedral
17	H(162)	C(38)	1.113	C(37)	109.441	C(39)	109.442	Pro-S
18	H(163)	C(38)	1.113	C(37)	109.462	C(39)	109.462	Pro-R
19	C(36)	C(37)	1.523	C(38)	109.5	C(39)	180	Dihedral
20	H(160)	C(37)	1.113	C(36)	109.442	C(38)	109.441	Pro-S
21	H(161)	C(37)	1.113	C(36)	109.462	C(38)	109.462	Pro-R
22	C(35)	C(36)	1.523	C(37)	109.5	C(38)	-180	Dihedral
23	H(158)	C(36)	1.113	C(35)	109.442	C(37)	109.442	Pro-S
24	H(159)	C(36)	1.113	C(35)	109.462	C(37)	109.462	Pro-R
25	C(34)	C(35)	1.523	C(36)	109.5	C(37)	-180	Dihedral
26	H(156)	C(35)	1.113	C(34)	109.443	C(36)	109.441	Pro-S
27	H(157)	C(35)	1.113	C(34)	109.461	C(36)	109.462	Pro-R
28	C(33)	C(34)	1.523	C(35)	109.501	C(36)	179.999	Dihedral
29	H(154)	C(34)	1.113	C(33)	109.44	C(35)	109.443	Pro-S
30	H(155)	C(34)	1.113	C(33)	109.462	C(35)	109.461	Pro-R
31	C(32)	C(33)	1.523	C(34)	109.501	C(35)	-180	Dihedral
32	H(152)	C(33)	1.113	C(32)	109.443	C(34)	109.44	Pro-S
33	H(153)	C(33)	1.113	C(32)	109.461	C(34)	109.463	Pro-R
34	C(31)	C(32)	1.523	C(33)	109.498	C(34)	-179.999	Dihedral
35	H(150)	C(32)	1.113	C(31)	109.446	C(33)	109.438	Pro-S
36	H(151)	C(32)	1.113	C(31)	109.463	C(33)	109.461	Pro-R
37	C(30)	C(31)	1.523	C(32)	109.498	C(33)	180	Dihedral
38	H(148)	C(31)	1.113	C(30)	109.439	C(32)	109.446	Pro-S
39	H(149)	C(31)	1.113	C(30)	109.461	C(32)	109.463	Pro-R
40	C(29)	C(30)	1.523	C(31)	109.501	C(32)	179.999	Dihedral
41	H(146)	C(30)	1.113	C(29)	109.44	C(31)	109.443	Pro-S
42	H(147)	C(30)	1.113	C(29)	109.459	C(31)	109.466	Pro-R
43	C(28)	C(29)	1.523	C(30)	109.501	C(31)	-180	Dihedral
44	H(144)	C(29)	1.113	C(28)	109.443	C(30)	109.44	Pro-S
45	H(145)	C(29)	1.113	C(28)	109.461	C(30)	109.462	Pro-R
46	C(27)	C(28)	1.523	C(29)	109.501	C(30)	-180	Dihedral
47	H(142)	C(28)	1.113	C(27)	109.44	C(29)	109.443	Pro-S
48	H(143)	C(28)	1.113	C(27)	109.462	C(29)	109.461	Pro-R
49	C(26)	C(27)	1.523	C(28)	109.501	C(29)	180	Dihedral
50	H(140)	C(27)	1.113	C(26)	109.443	C(28)	109.441	Pro-S
51	H(141)	C(27)	1.113	C(26)	109.461	C(28)	109.462	Pro-R
52	C(25)	C(26)	1.523	C(27)	109.498	C(28)	-180	Dihedral
53	H(138)	C(26)	1.113	C(25)	109.446	C(27)	109.438	Pro-S
54	H(139)	C(26)	1.113	C(25)	109.463	C(27)	109.461	Pro-R
55	C(22)	C(25)	1.523	C(26)	109.498	C(27)	-180	Dihedral
56	H(136)	C(25)	1.113	C(22)	109.438	C(26)	109.446	Pro-S
57	H(137)	C(25)	1.113	C(22)	109.461	C(26)	109.463	Pro-R
58	C(21)	C(22)	1.523	C(25)	109.501	C(26)	180	Dihedral
59	H(131)	C(22)	1.113	C(21)	109.44	C(25)	109.443	Pro-S
60	H(132)	C(22)	1.113	C(21)	109.459	C(25)	109.466	Pro-R
61	C(20)	C(21)	1.523	C(22)	109.501	C(25)	180	Dihedral
62	H(129)	C(21)	1.113	C(20)	109.443	C(22)	109.44	Pro-S
63	H(130)	C(21)	1.113	C(20)	109.461	C(22)	109.462	Pro-R
64	C(19)	C(20)	1.523	C(21)	109.501	C(22)	120.001	Dihedral

No	Atom	Bond Atom	Bond Length (Å)	Angle Atom	Angle (°)	2nd Angle Atom	2nd Angle (°)	2nd Angle Type
65	O(24)	C(20)	1.402	C(19)	109.442	C(21)	109.44	Pro-R
66	H(128)	C(20)	1.113	C(19)	109.461	C(21)	109.462	Pro-S
67	C(18)	C(19)	1.523	C(20)	109.499	C(21)	-119.998	Dihedral
68	C(23)	C(19)	1.523	C(18)	109.445	C(20)	109.442	Pro-S
69	H(127)	C(19)	1.113	C(18)	109.461	C(20)	109.46	Pro-R
70	C(17)	C(18)	1.523	C(19)	109.503	C(20)	59.999	Dihedral
71	H(125)	C(18)	1.113	C(17)	109.442	C(19)	109.442	Pro-R
72	H(126)	C(18)	1.113	C(17)	109.461	C(19)	109.461	Pro-S
73	C(16)	C(17)	1.523	C(18)	109.504	C(19)	180	Dihedral
74	H(123)	C(17)	1.113	C(16)	109.441	C(18)	109.443	Pro-R
75	H(124)	C(17)	1.113	C(16)	109.461	C(18)	109.462	Pro-S
76	C(15)	C(16)	1.523	C(17)	109.504	C(18)	180	Dihedral
77	H(121)	C(16)	1.113	C(15)	109.443	C(17)	109.441	Pro-R
78	H(122)	C(16)	1.113	C(15)	109.462	C(17)	109.461	Pro-S
79	C(14)	C(15)	1.523	C(16)	109.5	C(17)	180	Dihedral
80	H(119)	C(15)	1.113	C(14)	109.443	C(16)	109.442	Pro-R
81	H(120)	C(15)	1.113	C(14)	109.463	C(16)	109.461	Pro-S
82	C(13)	C(14)	1.523	C(15)	109.497	C(16)	180	Dihedral
83	H(117)	C(14)	1.113	C(13)	109.441	C(15)	109.442	Pro-R
84	H(118)	C(14)	1.113	C(13)	109.46	C(15)	109.461	Pro-S
85	C(12)	C(13)	1.523	C(14)	109.497	C(15)	180	Dihedral
86	H(115)	C(13)	1.113	C(12)	109.443	C(14)	109.444	Pro-R
87	H(116)	C(13)	1.113	C(12)	109.463	C(14)	109.463	Pro-S
88	C(11)	C(12)	1.523	C(13)	109.498	C(14)	180	Dihedral
89	H(113)	C(12)	1.113	C(11)	109.441	C(13)	109.442	Pro-R
90	H(114)	C(12)	1.113	C(11)	109.46	C(13)	109.461	Pro-S
91	C(10)	C(11)	1.523	C(12)	109.498	C(13)	180	Dihedral
92	H(111)	C(11)	1.113	C(10)	109.443	C(12)	109.444	Pro-R
93	H(112)	C(11)	1.113	C(10)	109.463	C(12)	109.463	Pro-S
94	C(9)	C(10)	1.523	C(11)	109.498	C(12)	180	Dihedral
95	H(109)	C(10)	1.113	C(9)	109.441	C(11)	109.442	Pro-R
96	H(110)	C(10)	1.113	C(9)	109.46	C(11)	109.461	Pro-S
97	C(8)	C(9)	1.523	C(10)	109.497	C(11)	180	Dihedral
98	H(107)	C(9)	1.113	C(8)	109.442	C(10)	109.441	Pro-R
99	H(108)	C(9)	1.113	C(8)	109.463	C(10)	109.463	Pro-S
100	C(7)	C(8)	1.523	C(9)	109.497	C(10)	180	Dihedral
101	H(105)	C(8)	1.113	C(7)	109.441	C(9)	109.442	Pro-R
102	H(106)	C(8)	1.113	C(7)	109.46	C(9)	109.461	Pro-S
103	C(6)	C(7)	1.523	C(8)	109.497	C(9)	180	Dihedral
104	H(103)	C(7)	1.113	C(6)	109.442	C(8)	109.441	Pro-R
105	H(104)	C(7)	1.113	C(6)	109.463	C(8)	109.463	Pro-S
106	C(5)	C(6)	1.523	C(7)	109.497	C(8)	180	Dihedral
107	H(101)	C(6)	1.113	C(5)	109.441	C(7)	109.442	Pro-R
108	H(102)	C(6)	1.113	C(5)	109.46	C(7)	109.462	Pro-S
109	C(4)	C(5)	1.523	C(6)	109.497	C(7)	180	Dihedral
110	H(99)	C(5)	1.113	C(4)	109.442	C(6)	109.441	Pro-R
111	H(100)	C(5)	1.113	C(4)	109.463	C(6)	109.463	Pro-S
112	C(3)	C(4)	1.523	C(5)	109.497	C(6)	180	Dihedral
113	H(97)	C(4)	1.113	C(3)	109.441	C(5)	109.442	Pro-R
114	H(98)	C(4)	1.113	C(3)	109.46	C(5)	109.462	Pro-S
115	C(2)	C(3)	1.523	C(4)	109.497	C(5)	180	Dihedral
116	H(95)	C(3)	1.113	C(2)	109.443	C(4)	109.44	Pro-R
117	H(96)	C(3)	1.113	C(2)	109.464	C(4)	109.463	Pro-S
118	C(1)	C(2)	1.523	C(3)	109.497	C(4)	180	Dihedral
119	H(93)	C(2)	1.113	C(1)	109.44	C(3)	109.443	Pro-R
120	H(94)	C(2)	1.113	C(1)	109.459	C(3)	109.462	Pro-S
121	C(45)	C(44)	1.523	C(43)	109.5	C(42)	60	Dihedral
122	C(46)	C(44)	1.523	C(43)	109.442	C(45)	109.442	Pro-S
123	H(172)	C(44)	1.113	C(43)	109.462	C(45)	109.462	Pro-R
124	C(77)	O(24)	1.402	C(20)	106.8	C(19)	-179.996	Dihedral
125	C(78)	C(45)	1.523	C(44)	109.5	C(43)	-120	Dihedral
126	H(173)	C(45)	1.113	C(44)	109.442	C(78)	109.442	Pro-S
127	H(174)	C(45)	1.113	C(44)	109.462	C(78)	109.462	Pro-R
128	C(79)	C(78)	1.523	C(45)	109.5	C(44)	180	Dihedral
129	H(234)	C(78)	1.113	C(45)	109.442	C(79)	109.442	Pro-S
130	H(235)	C(78)	1.113	C(45)	109.462	C(79)	109.462	Pro-R
131	C(80)	C(79)	1.523	C(78)	109.5	C(45)	180	Dihedral
132	H(236)	C(79)	1.113	C(78)	109.442	C(80)	109.442	Pro-S
133	H(237)	C(79)	1.113	C(78)	109.462	C(80)	109.462	Pro-R
134	C(81)	C(80)	1.523	C(79)	109.5	C(78)	-180	Dihedral
135	H(238)	C(80)	1.113	C(79)	109.442	C(81)	109.442	Pro-S
136	H(239)	C(80)	1.113	C(79)	109.462	C(81)	109.462	Pro-R
137	C(82)	C(81)	1.523	C(80)	109.5	C(79)	-180	Dihedral
138	H(240)	C(81)	1.113	C(80)	109.442	C(82)	109.442	Pro-S
139	H(241)	C(81)	1.113	C(80)	109.461	C(82)	109.462	Pro-R
140	C(83)	C(82)	1.523	C(81)	109.5	C(80)	180	Dihedral
141	H(242)	C(82)	1.113	C(81)	109.442	C(83)	109.442	Pro-S
142	H(243)	C(82)	1.113	C(81)	109.462	C(83)	109.462	Pro-R
143	C(84)	C(83)	1.523	C(82)	109.5	C(81)	180	Dihedral
144	H(244)	C(83)	1.113	C(82)	109.442	C(84)	109.442	Pro-S
145	H(245)	C(83)	1.113	C(82)	109.462	C(84)	109.462	Pro-R
146	C(85)	C(84)	1.523	C(83)	109.5	C(82)	-180	Dihedral
147	H(246)	C(84)	1.113	C(83)	109.461	C(85)	109.461	Pro-R
148	H(247)	C(84)	1.113	C(83)	109.461	C(85)	109.461	Pro-R
149	C(86)	C(85)	1.523	C(84)	109.5	C(83)	-179.999	Dihedral
150	H(248)	C(85)	1.113	C(84)	109.442	C(86)	109.442	Pro-S
151	H(249)	C(85)	1.113	C(84)	109.462	C(86)	109.462	Pro-R
152	C(87)	C(86)	1.523	C(85)	109.5	C(84)	180	Dihedral
153	H(250)	C(86)	1.113	C(85)	109.442	C(87)	109.442	Pro-S
154	H(251)	C(86)	1.113	C(85)	109.462	C(87)	109.462	Pro-R
155	C(88)	C(87)	1.523	C(86)	109.5	C(85)	179.999	Dihedral

No	Atom	Bond Atom	Bond Length (Å)	Angle Atom	Angle (°)	2nd Angle Atom	2nd Angle (°)	2nd Angle Type
156	H(252)	C(87)	1.113	C(86)	109.442	C(88)	109.442	Pro-S
157	H(253)	C(87)	1.113	C(86)	109.461	C(88)	109.462	Pro-R
158	C(89)	C(88)	1.523	C(87)	109.5	C(86)	180	Dihedral
159	H(254)	C(88)	1.113	C(87)	109.442	C(89)	109.442	Pro-S
160	H(255)	C(88)	1.113	C(87)	109.462	C(89)	109.462	Pro-R
161	C(51)	C(89)	1.523	C(88)	109.502	C(87)	180	Dihedral
162	H(256)	C(89)	1.113	C(51)	109.44	C(88)	109.443	Pro-S
163	H(257)	C(89)	1.113	C(51)	109.462	C(88)	109.461	Pro-R
164	C(49)	C(51)	1.523	C(89)	109.497	C(88)	60	Dihedral
165	O(52)	C(51)	1.402	C(49)	109.442	C(89)	109.441	Pro-S
166	H(180)	C(51)	1.113	C(49)	109.463	O(52)	109.524	Pro-S
167	C(48)	C(49)	1.509	C(51)	109.501	O(52)	-120.037	Dihedral
168	C(53)	C(49)	1.523	C(48)	109.442	C(51)	109.443	Pro-S
169	H(179)	C(49)	1.113	C(48)	109.461	C(51)	109.461	Pro-R
170	C(47)	C(48)	1.338	C(49)	120.002	C(51)	-180	Dihedral
171	O(50)	C(48)	1.208	O(47)	119.999	C(49)	119.999	Pro-R
172	C(54)	C(53)	1.523	C(49)	109.5	C(48)	119.999	Dihedral
173	H(182)	C(53)	1.113	C(49)	109.441	C(54)	109.444	Pro-S
174	H(183)	C(53)	1.113	C(49)	109.463	C(54)	109.46	Pro-R
175	C(55)	C(54)	1.523	C(53)	109.5	C(49)	-180	Dihedral
176	H(184)	C(54)	1.113	C(53)	109.441	C(55)	109.443	Pro-S
177	H(185)	C(54)	1.113	C(53)	109.462	C(55)	109.461	Pro-R
178	C(56)	C(55)	1.523	C(54)	109.5	C(53)	180	Dihedral
179	H(186)	C(55)	1.113	C(54)	109.442	C(56)	109.442	Pro-S
180	H(187)	C(55)	1.113	C(54)	109.462	C(56)	109.462	Pro-R
181	C(57)	C(56)	1.523	C(55)	109.5	C(54)	180	Dihedral
182	H(188)	C(56)	1.113	C(55)	109.442	C(57)	109.442	Pro-S
183	H(189)	C(56)	1.113	C(55)	109.462	C(57)	109.462	Pro-R
184	C(58)	C(57)	1.523	C(56)	109.5	C(55)	-60	Dihedral
185	H(190)	C(57)	1.113	C(56)	109.442	C(58)	109.442	Pro-R
186	H(191)	C(57)	1.113	C(56)	109.462	C(58)	109.462	Pro-S
187	C(59)	C(58)	1.523	C(57)	109.5	C(56)	-180	Dihedral
188	H(192)	C(58)	1.113	C(57)	109.442	C(59)	109.442	Pro-R
189	H(193)	C(58)	1.113	C(57)	109.462	C(59)	109.462	Pro-S
190	C(60)	C(59)	1.523	C(58)	109.5	C(57)	180	Dihedral
191	H(194)	C(59)	1.113	C(58)	109.442	C(60)	109.442	Pro-R
192	H(195)	C(59)	1.113	C(58)	109.462	C(60)	109.462	Pro-S
193	C(61)	C(60)	1.523	C(59)	109.5	C(58)	180	Dihedral
194	H(196)	C(60)	1.113	C(59)	109.442	C(61)	109.442	Pro-R
195	H(197)	C(60)	1.113	C(59)	109.462	C(61)	109.462	Pro-S
196	C(62)	C(61)	1.523	C(60)	109.5	C(59)	179.999	Dihedral
197	H(198)	C(61)	1.113	C(60)	109.442	C(62)	109.441	Pro-R
198	H(199)	C(61)	1.113	C(60)	109.462	C(62)	109.462	Pro-S
199	C(63)	C(62)	1.523	C(61)	109.5	C(60)	180	Dihedral
200	H(200)	C(62)	1.113	C(61)	109.442	C(63)	109.442	Pro-R
201	H(201)	C(62)	1.113	C(61)	109.462	C(63)	109.462	Pro-S
202	C(64)	C(63)	1.523	C(62)	109.5	C(61)	-180	Dihedral
203	H(202)	C(63)	1.113	C(62)	109.442	C(64)	109.442	Pro-R
204	H(203)	C(63)	1.113	C(62)	109.462	C(64)	109.462	Pro-S
205	C(65)	C(64)	1.523	C(63)	109.5	C(62)	180	Dihedral
206	H(204)	C(64)	1.113	C(63)	109.442	C(65)	109.442	Pro-R
207	H(205)	C(64)	1.113	C(63)	109.462	C(65)	109.462	Pro-S
208	C(66)	C(65)	1.523	C(64)	109.5	C(63)	-180	Dihedral
209	H(206)	C(65)	1.113	C(64)	109.442	C(66)	109.442	Pro-R
210	H(207)	C(65)	1.113	C(64)	109.462	C(66)	109.462	Pro-S
211	C(67)	C(66)	1.523	C(65)	109.5	C(64)	-180	Dihedral
212	H(208)	C(66)	1.113	C(65)	109.442	C(67)	109.442	Pro-R
213	H(209)	C(66)	1.113	C(65)	109.461	C(67)	109.462	Pro-S
214	C(68)	C(67)	1.523	C(66)	109.5	C(65)	180	Dihedral
215	H(210)	C(67)	1.113	C(66)	109.442	C(68)	109.442	Pro-R
216	H(211)	C(67)	1.113	C(66)	109.462	C(68)	109.462	Pro-S
217	C(69)	C(68)	1.523	C(67)	109.5	C(66)	-180	Dihedral
218	H(212)	C(68)	1.113	C(67)	109.442	C(69)	109.442	Pro-R
219	H(213)	C(68)	1.113	C(67)	109.462	C(69)	109.462	Pro-S
220	C(70)	C(69)	1.523	C(68)	109.5	C(67)	-180	Dihedral
221	H(214)	C(69)	1.113	C(68)	109.442	C(70)	109.442	Pro-R
222	H(215)	C(69)	1.113	C(68)	109.462	C(70)	109.462	Pro-S
223	C(71)	C(70)	1.523	C(69)	109.5	C(68)	-180	Dihedral
224	H(216)	C(70)	1.113	C(69)	109.442	C(71)	109.442	Pro-R
225	H(217)	C(70)	1.113	C(69)	109.462	C(71)	109.462	Pro-S
226	C(72)	C(71)	1.523	C(70)	109.5	C(69)	180	Dihedral
227	H(218)	C(71)	1.113	C(70)	109.442	C(72)	109.442	Pro-R
228	H(219)	C(71)	1.113	C(70)	109.462	C(72)	109.462	Pro-S
229	C(73)	C(72)	1.523	C(71)	109.5	C(70)	180	Dihedral
230	H(220)	C(72)	1.113	C(71)	109.442	C(73)	109.442	Pro-R
231	H(221)	C(72)	1.113	C(71)	109.461	C(73)	109.462	Pro-S
232	C(74)	C(73)	1.523	C(72)	109.5	C(71)	180	Dihedral
233	H(222)	C(73)	1.113	C(72)	109.442	C(74)	109.442	Pro-R
234	H(223)	C(73)	1.113	C(72)	109.463	C(74)	109.46	Pro-S
235	C(75)	C(74)	1.523	C(73)	109.5	C(72)	-179.999	Dihedral
236	H(224)	C(74)	1.113	C(73)	109.443	C(75)	109.441	Pro-R
237	H(225)	C(74)	1.113	C(73)	109.46	C(75)	109.463	Pro-S
238	C(76)	C(75)	1.523	C(74)	109.5	C(73)	-180	Dihedral
239	H(226)	C(75)	1.113	C(74)	109.446	C(76)	109.44	Pro-R
240	H(227)	C(75)	1.113	C(74)	109.463	C(76)	109.459	Pro-S
241	H(90)	C(1)	1.113	C(2)	109.499	C(3)	180	Dihedral
242	H(91)	C(1)	1.113	C(2)	109.444	H(90)	109.438	Pro-S
243	H(92)	C(1)	1.113	C(2)	109.462	H(90)	109.463	Pro-R
244	H(133)	C(23)	1.113	C(19)	109.503	C(18)	-179.999	Dihedral
245	H(134)	C(23)	1.113	C(19)	109.442	H(133)	109.442	Pro-R
246	H(135)	C(23)	1.113	C(19)	109.463	H(133)	109.461	Pro-S

No	Atom	Bond Atom	Bond Length (Å)	Angle Atom	Angle (º)	2nd Angle Atom	2nd Angle (º)	2nd Angle Type
247	H(175)	C(46)	1.113	C(44)	109.5	C(43)	180	Dihedral
248	H(176)	C(46)	1.113	C(44)	109.442	H(175)	109.442	Pro-R
249	H(177)	C(46)	1.113	C(44)	109.462	H(175)	109.462	Pro-S
250	H(178)	O(47)	0.972	C(48)	106.099	C(49)	179.999	Dihedral
251	H(181)	O(52)	0.942	C(51)	106.901	C(49)	-179.998	Dihedral
252	H(228)	C(76)	1.113	C(75)	109.502	C(74)	179.998	Dihedral
253	H(229)	C(76)	1.113	C(75)	109.443	H(228)	109.438	Pro-R
254	H(230)	C(76)	1.113	C(75)	109.463	H(228)	109.46	Pro-S
255	H(231)	C(77)	1.113	O(24)	109.499	C(20)	-179.999	Dihedral
256	H(232)	C(77)	1.113	O(24)	109.439	H(231)	109.441	Pro-S
257	H(233)	C(77)	1.113	O(24)	109.466	H(231)	109.463	Pro-R

The table demonstrates the effect of the configuration in the results of internal coordinate and indicates that the ψ angles of MA (1) were in the range (±180). Though, the MM2.11 is a method for calculating E of a molecule, and for the program to try to optimize the structure such as minimize E by stretching or contracting bonds lengths, opening and closing of angles, and twisting around single bonds.11 MM2 treats bonds as springs which can be stretched, bend or twisted. Therefore, the MM2 properties was intended for MA (1), the results were showed that the stretch; bend; stretch-bend; torsion; non-1,4 VDW; 1,4 VDW and the total energy were equal to 0.3944; 10.5258; 0.0714; 13.3334; 131.8099; 98.8838 and 255.0187 kcal/mol respectively. A high VDW interaction of this molecule was observed, due to the results of dipole/ dipole was not computed. Antigen-antibody bond the immunological property of greatest significance is the specificity of the combining power of antibody for the immunizing antigen.12 The forces of VDW attraction, hydrogen-bond formation, and interaction of electrically charged groups are in themselves not specific; each atom of a molecule attracts every other atom of another molecule by VDW attraction, each hydrogen atom attached to an electronegative atom attracts every other electronegative atom with an unshared electron pair which comes near it.12 Though, the MM2 minimization for MA (1) was calculated. The results were showed that the stretch; bend; stretch-bend; torsion; non-1,4 VDW; 1,4 VDW, dipole/ dipole and the total energy were equal to 7.1443; 15.3535; 2.2868; 8.8418; 33.3460; 62.4862; 0.2185 and 62.9851 kcal/mol respectively. These results were showed that the minimization was attended successfully.

GN Ramachandran,13 used computer models of small polypeptides to systematically vary and with the objective of finding stable conformations. For each conformation, the structure was examined for close contacts between atoms. Atoms were treated as hard spheres with dimensions corresponding to their van der Waals radii. Thus, the close contact of atoms in lipid structure were calculated before and after minimization, see table (4) below.

Table 4. Close contact of atoms in MA (1)

No	Atoms	Before minimization	After minimization
		Actual close contact atoms Å	
1	H(128)-H(233)	2.222	2.329
2	C(20)-H(233)	2.498	2.612
3	H(129)-H(232)	1.612	2.395
4	C(20)-H(232)	2.498	2.771
5	C(21)-H(232)	2.252	2.720
6	O(24)-H(135)	2.399	2.808
7	O(24)-H(133)	2.398	2.484
8	H(236)-H(205)	2.186	2.841
9	H(240)-H(201)	1.861	3.100
10	H(247)-H(197)	1.921	2.508
11	H(243)-H(197)	2.061	2.832
12	H(247)-H(193)	2.058	3.075
13	H(186)-H(192)	1.84	2.219
14	C(55)-H(192)	2.522	2.883
15	H(186)-C(58)	2.522	2.871
16	H(255)-H(186)	2.173	2.451
17	H(251)-H(186)	1.943	2.914
18	H(255)-H(185)	1.601	2.150
19	C(88)-H(185)	2.521	3.097
20	H(255)-C(55)	2.465	2.994
21	C(48)-H(183)	2.425	2.584
22	H(257)-H(182)	1.596	2.293
23	C(51)-H(182)	2.431	2.806
24	H(255)-H(182)	1.245	2.415
25	C(89)-H(182)	1.812	2.687
26	C(88)-H(182)	1.704	2.916
27	C(87)-H(182)	2.543	3.509

No	Atoms	Before minimization	After minimization
		Actual close contact atoms Å	
28	H(179)-C(54)	2.434	2.734
29	H(255)-C(54)	1.828	2.670
30	H(180)-O(50)	2.066	2.710
31	C(51)-O(50)	2.650	2.898
32	O(52)-H(179)	2.376	2.497
33	H(257)-C(53)	2.408	2.958
34	H(255)-C(53)	1.705	2.800
35	C(89)-C(53)	2.538	3.096
36	C(88)-C(53)	2.488	3.437
37	H(180)-C(48)	2.426	2.576
38	H(255)-C(49)	2.522	3.249
39	C(46)-H(174)	2.432	2.629
40	C(43)-H(173)	2.42	2.671
41	C(42)-H(173)	2.588	3.674
42	H(172)-C(78)	2.433	2.694
43	H(128)-C(77)	2.498	2.592
44	H(129)-C(77)	2.364	2.891
45	C(21)-C(77)	2.700	2.945
46	H(128)-H(123)	1.838	2.612
47	C(20)-H(123)	2.522	2.868
48	H(131)-H(123)	1.921	2.274
49	H(128)-C(17)	2.522	3.113
50	H(130)-H(127)	1.882	2.308
51	C(21)-H(127)	2.433	2.609
52	O(24)-C(23)	2.499	2.672
53	H(128)-C(18)	2.433	2.606
54	C(22)-H(128)	2.433	2.628
55	H(129)-O(24)	2.376	2.491
56	H(130)-C(19)	2.433	2.574
57	O(47)-H(179)		2.436

The table shows that the shortest non-bonded contact was equal to 1.705 Å, this was seems to be higher than the closest allowed contact distance in the acid structure. For example the maximum deviation of close contact H(255)-C(53) atoms which equal to 1.705 Å from C-H bond which equal to 1.113 Å was corresponds to about 0.592. The results after minimization as seen in table (4) were showed significant increase in the actual close contact atoms. Also, the results were displayed that the carboxylic O(47) atom was close contact with H(179) atom that bonded with alkane C(49) atom in mycolic motif after minimization.

The MMFF94 energy and gradient for MA (1) were also intended. The results were showed that the total energy and RMS gradient for this frame were equal to 228.561 kcal/mol and 17.735 respectively. Thus, the MMFF94 minimization iteration which is terminated normally because the gradient norm is less than the minimum gradient norm was also envisioned. The results were showed that the final energy was equal to 11.2963 kcal/mol. However, the results of MMFF94 minimization/sampling which calculated for MA (1) were showed that the final energy was equal to 11.1221 kcal/mol. These results also displayed that the minimization was attended successfully.

Summary

This study focused in area of molecular mechanics, in order to study the detailed structure and physical properties of *trans*-alkene MA. Molecular mechanics calculates the energy of a molecule and then adjusts the energy through changes in the bonds length and angle to obtain the minimum energy structure. Also, the ψ, E and ICM results were gave some advantages for suggesting new derivatives. One hops that the folding behavior of *trans*-alkene MA or its derivative may better mimic to the actual folding process in nature.

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