Molecular Simulations of Dodecyl-β-maltoside Micelles in Water: Influence of the Headgroup Conformation and Force field Parameters

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Figures

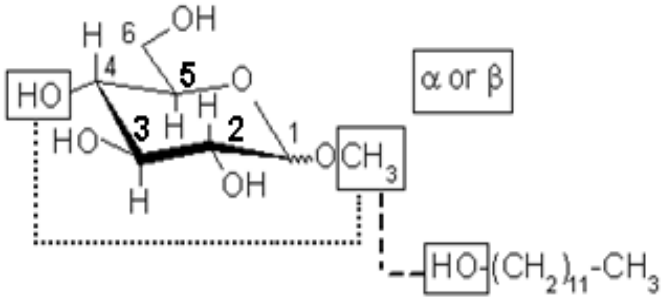

Figure S1: RESP charge derivation for the α- and β-anomers of $C_{12}G_2$ glycolipids. Computational conditions, RESP charge values, force field libraries as well as optimized geometries were submitted in the R.E.DD.B. database (http://q4md-forcefieldtools.org/REDDB/) and are available under the "F-72" R.E.DD.B code. Intra- and inter-molecular charge constraints used during the fitting step are represented using fine dashed and dashed lines, respectively. This allows defining the molecular fragments required for the construction of the α- and β-anomers of C12G2 surfactants.

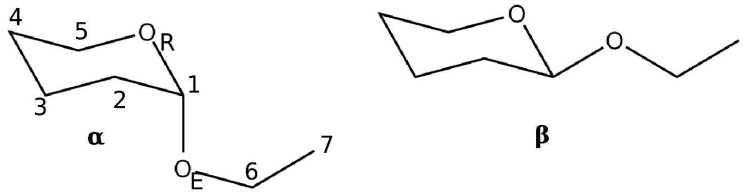

Figure S2: Model compounds used in dihedral force field parameter development.

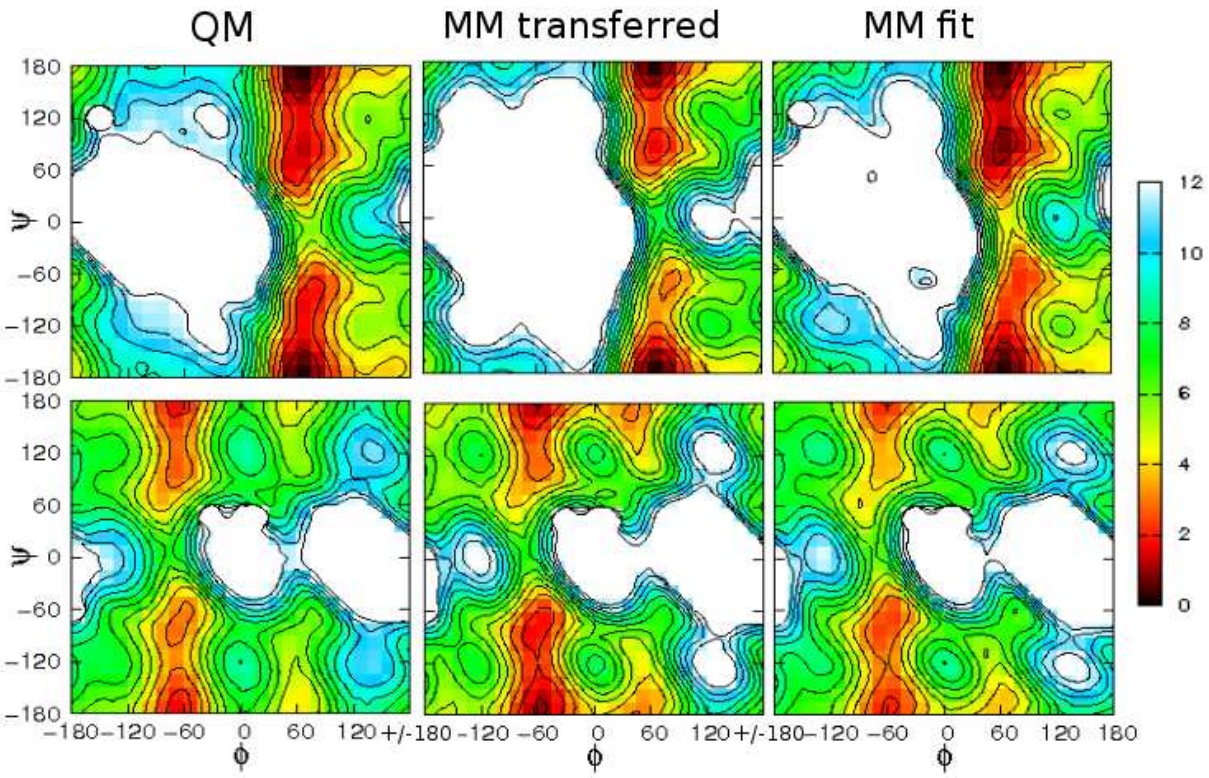

Figure S3: Φ-Ψ potential energy surfaces in quantum and molecular mechanics (QM and MM) representations for α- (top) and β- (bottom) ethoxy-THP. Energies are in kcal/mol, with contours every 1kcal/mol.

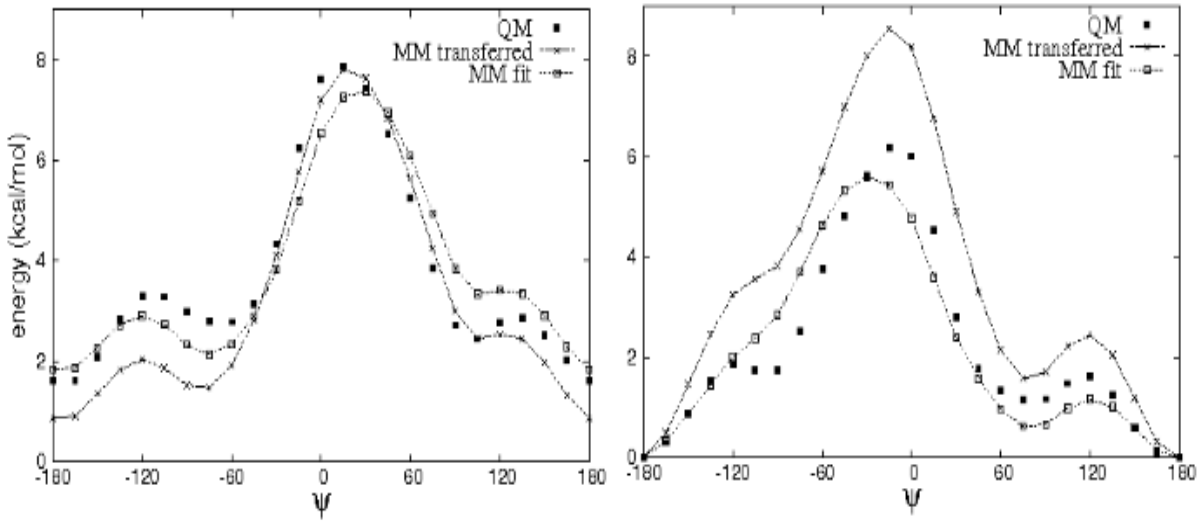

Figure S4: Quantum and molecular mechanics transferred and MM fit energies as a function of ψ for α- (at **Φ**=+60) (right) and β-anomers (at **Φ**=-60) (left)

				Partial charges (qe-)		
	atom names	atom types	Mol. Type*	**α**-anomer	Mol. Type*	**β**-anomer
GlcA	C1	CG	AMT	0.5393	AMT	0.5393
	O1	OS		-0.5101		-0.5101
	C2	CG		0.0788		0.0788
	O2	OH		-0.6792		-0.6792
	H2Oa	HO		0.4380		0.4380
	C3	CG		0.5723		0.5723
	O3	OH		-0.7472		-0.7472
	H3Oa	HO		0.4303		0.4303
	C4	CG		0.1852		0.1852
	O4	OH		-0.6469		-0.6469
	H4Oa	HO		0.3851		0.3851
	C5	CG		0.2313		0.2313
	O5	OS		-0.5572		-0.5572
	C6	CG		0.2326		0.2326
	O6	OH		-0.6166		-0.6166
	HO6	HO		0.4025		0.4025
	H1	H2		0.0000		0.0000
	H1a, H2a, H3a, H4a, H5a, H6a, H6b	H1		0.0000		0.0000
GlcB	C1	CG	AMG	0.5393	BMG	0.3005
	O1	OS		-0.5101		-0.4456
	C2	CG		0.0788		0.4091
	O2	OH		-0.6792		-0.7057
	H2Oa	HO		0.4380		0.4094
	C3	CG		0.5723		0.2633
	O3	OH		-0.7472		-0.7099
	H3Oa	HO		0.4303		0.4342
	C4	CG		0.1852		0.3272
	C5	CG		0.2313		0.0974
	O5	OH		-0.5572		-0.4067
	C6	CG		0.2326		0.2389
	O6	OS		-0.6166		-0.6200
	H6Oa	OS		0.4025		0.4079
	H1	H2		0.0000		0.0000
	H1a, H2a, h3a, H4b, H5a, H6a, H6b	H1		0.0000		0.0000
DOD	C7	CG	C12	0.1842	C12	0.1842
	H 7a, H 7b	HC		0.0000		0.0000
	C8	CG		0.1245		0.1245
	H8a, H8b	HC		0.0000		0.0000
	C9	CG		-0.0562		-0.0562
	H9a, H9b	HC		0.0000		0.0000
	C10	CG		-0.0066		-0.0066
	H10a, H10b	HC		0.0000		0.0000
	C11	CG		0.0175		0.0175
	H11a, H11b	HC		0.0000		0.0000
	C12	CG		0.0029		0.0029
	H12a, H12b	HC		0.0000		0.0000
	C13	CG		-0.0031		-0.0031
	H13a, H13b	HC		0.0000		0.0000
	C14	CG		-0.0016		-0.0016
	H14a, H14b	HC		0.0000		0.0000
	C15	CG		-0.0092		-0.0092
	H15a, H15b	HC		0.0000		0.0000
	C16	CG		0.0171		0.0171
	H16a, H16b	HC		0.0000		0.0000
	C17	CG		0.0131		0.0131
	H17a, H17b	HC		0.0000		0.0000
	C18	CG		-0.0208		-0.0208
	H18a, H18b, H18c	HC		0.0000		0.0000

Table S1: RESP atomic charges for the α- and β-anomers of $C_{12}G_2$ GL. Atom types are these defined in the GLYCAM06 force field. *See Figure S1 and project "F72" in the RED.DB for details for the position of each atom and molecule type in the $C_{12}G_2$ GL molecule.

model compound	valence angle / dihedral angle / bond length[a]	QM	MM	MM-QM
α	C_1-O_{link}	1.41	1.40	-0.01
	O_{link}-C6	1.43	1.42	-0.01
	C6-C7	1.51	1.53	0.01
	O_{ring}-C_1-O_{link}	112.0	110.52	-1.48
	C2-C_1-O_{link}	107.0	108.77	1.77
	C1-OE-C6	112.8	112.15	-0.65
	OE-C6-C7	107.2	108.46	1.26
	Φ	61.64	63.22	1.7
	Ψ	175.08	178.58	3.5
β	C_1-O_{link}	1.39	1.40	0.01
	O_{link}-C6	1.43	1.42	-0.01
	C6-C7	1.51	1.53	0.01
	O_{ring}-C_1-O_{link}	108.3	110.2	1.9
	C2-C_1-O_{link}	108.6	106.9	-1.7
	C1-OE-C6	113.1	112.1	-1.0
	OE-C6-C7	107.0	108.5	1.5
	Φ	-63.2	-59.0	4.2
	Ψ	-172.0	-172.8	-0.8
		bonds	average	0.00
			RMSE	0.01
		angles	average	0.2
			RMSE	1.5

Table S2: Fully optimized QM and MM geometries for the model compounds.

model com-pound	water orien-tation[a]	energy (kcal/mol)			distance (Å)		
		1.16*HF[b]	MM	MM-QM	HF-0.20[b]	MM	MM-QM
α	-90	-4.73	-4.50	0.23	1.92	2.02	0.10
	0	-6.04	-5.78	0.26	1.86	1.81	-0.05
	90	-4.04	-4.13	-0.09	2.02	2.03	0.01
β	0	-6.17	-5.52	0.65	1.86	1.82	-0.04
	90	-5.66	-5.42	0.24	1.85	1.79	-0.06
	180	-6.43	-6.08	0.35	1.86	1.8	-0.06
	average			0.27			-0.02
	RMSE			0.35			0.06

Table S3: Solute:water pair interaction energies and distances for the model compounds.

	CHARMM-K							
	α-$C_{12}G_2$				β-$C_{12}G_2$			
	headgroup-solvent		Inter-headgroup		headgroup-solvent		Inter-headgroup	
	frac. donor	frac. acceptor	Selection [a]	frac. donor	frac. donor	frac. acceptor	Selection [a]	frac. donor
O_1	-	0.41 ± 0.06	O_2-H...O_1	~ 0	-	0.43 ± 0.04	O_2-H...O_1	~ 0
O_2	0.77 ± 0.05	0.85 ± 0.07	O_2-H...O_3	~ 0	0.75 ± 0.04	1.00 ± 0.06	O_2-H...O_3	~ 0
O_3	0.77 ± 0.06	1.05 ± 0.07	O_3-H...O_2	0.01 ± 0.01	0.85 ± 0.07	1.06 ± 0.03	O_3-H...O_2	0.03 ± 0.01
O_4	0.83 ± 0.05	0.78 ± 0.07	O_3-H...O_4	0.01 ± 0.01	0.87 ± 0.04	0.95 ± 0.06	O_3-H...O_4	0.01 ± 0.01
O_5	-	0.47 ± 0.06	O_4-H...O_3	~ 0	-	0.40 ± 0.05	O_4-H...O_3	~ 0
O_6	0.84 ± 0.05	1.43 ± 0.08	O_4-H...O_5	~ 0	0.77 ± 0.04	1.30 ± 0.06	O_4-H...O_5	~ 0
O_7	-	0.14 ± 0.03	O_4-H...O_6	0.02 ± 0.01	-	0.18 ± 0.03	O_4-H...O_6	0.02 ± 0.01
O_8	0.66 ± 0.06	0.90 ± 0.07	O_6-H...O_4	0.03 ± 0.02	0.49 ± 0.04	0.73 ± 0.06	O_6-H...O_4	0.03 ± 0.01
O_9	0.70 ± 0.05	0.93 ± 0.06	O_6-H...O_5	~ 0	0.66 ± 0.04	0.73 ± 0.05	O_6-H...O_5	0.01 ± 0.01
O_{10}	-	0.29 ± 0.05	O_8-H...O_9	~ 0	-	0.33 ± 0.04	O_8-H...O_9	0.04 ± 0.01
O_{11}	0.65 ± 0.06	0.96 ± 0.07	O_8-H...O_{10}	0.01 ± 0.01	0.52 ± 0.04	0.87 ± 0.06	O_8-H...O_{10}	0.03 ± 0.01
Total	5.22 ± 0.06	8.21 ± 0.07	O_{11}-H...O_{10}	0.02 ± 0.01	4.91 ± 0.04	7.98 ± 0.05	O_{11}-H...O_{10}	0.02 ± 0.01
Total	13.43 ± 0.07			0.10 ± 0.01	12.9 ± 0.05			0.19 ± 0.01

Table S4: Average number hydrogen bonds (HB) per surfactant between the water molecules and the maltose headgroup and between selected atoms belonging to the surfactant head groups. The HB distance (O…O) = 3.5 Å and angle O-H…O is from 120° to 180° (Umemura, Yuguchi *et al.* 2005) [a] and partially those computed by ref. (Chong, Hashim *et al.* 2006).

	CHARMM-Opt							
	α-$C_{12}G_2$				β-$C_{12}G_2$			
	headgroup-solvent		Inter-headgroup		headgroup-solvent		Inter-headgroup	
	frac. donor	frac. acceptor	Selection [a]	frac. donor	frac. donor	frac. acceptor	Selection [a]	frac. donor
O_1	-	0.30 ± 0.05	O_2-H...O_1	~ 0	-	0.33 ± 0.04	O_2-H...O_1	~ 0
O_2	0.65 ± 0.06	0.88 ± 0.08	O_2-H...O_3	~ 0	0.70 ± 0.04	0.87 ± 0.06	O_2-H...O_3	~ 0
O_3	0.78 ± 0.05	1.14 ± 0.08	O_3-H...O_2	0.02 ± 0.01	0.84 ± 0.04	1.14 ± 0.06	O_3-H...O_2	0.02 ± 0.01
O_4	0.81 ± 0.05	0.80 ± 0.07	O_3-H...O_4	~ 0	0.85 ± 0.04	0.93 ± 0.06	O_3-H...O_4	0.02 ± 0.01
O_5	-	0.42 ± 0.06	O_4-H...O_3	~ 0	-	0.35 ± 0.04	O_4-H...O_3	~ 0
O_6	0.75 ± 0.06	1.20 ± 0.08	O_4-H...O_5	~ 0	0.67 ± 0.04	1.12 ± 0.06	O_4-H...O_5	~ 0
O_7	-	0.08 ± 0.03	O_4-H...O_6	0.02 ± 0.02	-	0.12 ± 0.03	O_4-H...O_6	0.02 ± 0.01
O_8	0.56 ± 0.06	0.76 ± 0.07	O_6-H...O_4	0.02 ± 0.02	0.44 ± 0.04	0.65 ± 0.05	O_6-H...O_4	0.02 ± 0.01
O_9	0.56 ± 0.06	0.87 ± 0.07	O_6-H...O_5	~ 0	0.52 ± 0.04	0.71 ± 0.05	O_6-H...O_5	~ 0
O_{10}	-	0.25 ± 0.05	O_8-H...O_9	0.02 ± 0.02	-	0.27 ± 0.04	O_8-H...O_9	0.05 ± 0.01
O_{11}	0.46 ± 0.05	0.83 ± 0.08	O_8-H...O_{10}	0.02 ± 0.02	0.70 ± 0.04	0.76 ± 0.05	O_8-H...O_{10}	0.04 ± 0.01
Total	4.55 ± 0.06	7.53 ± 0.06	O_{11}-H...O_{10}	0.02 ± 0.02	4.72 ± 0.04	7.25 ± 0.05	O_{11}-H...O_{10}	0.04 ± 0.01
Total	12.08 ± 0.06			0.12 ± 0.02	11.97 ± 0.04			0.21 ± 0.01

Table S5: Average number hydrogen bonds (HB) per surfactant between the water molecules and the maltose headgroup and between selected atoms belonging to the surfactant head groups. The HB distance (O…O) = 3.5 Å and angle O-H…O is from 120° to 180° (Umemura, Yuguchi *et al.* 2005) [a] and partially those computed by ref. (Chong, Hashim *et al.* 2006).

	GLYCAM06							
	α-$C_{12}G_2$				β-$C_{12}G_2$			
	headgroup-solvent		Inter-headgroup		headgroup-solvent		Inter-headgroup	
	frac. donor	frac. acceptor	Selection [a]	frac. donor	frac. donor	frac. acceptor	Selection [a]	frac. donnor
O_1	-	0.24 ± 0.04	O_2-H...O_1	~ 0	-	0.19 ± 0.03	O_2-H...O_1	~ 0
O_2	0.76 ± 0.05	0.69 ± 0.07	O_2-H...O_3	0.03 ± 0.02	0.78 ± 0.03	0.84 ± 0.05	O_2-H...O_3	0.01 ± 0.01
O_3	0.66 ± 0.06	0.96 ± 0.07	O_3-H...O_2	0.02 ± 0.02	0.40 ± 0.04	1.13 ± 0.05	O_3-H...O_2	0.03 ± 0.01
O_4	0.69 ± 0.05	0.62 ± 0.07	O_3-H...O_4	0.02 ± 0.01	0.84 ± 0.04	0.87 ± 0.06	O_3-H...O_4	0.02 ± 0.01
O_5	-	0.68 ± 0.06	O_4-H...O_3	0.02 ± 0.01	-	0.46 ± 0.04	O_4-H...O_3	~ 0
O_6	0.73 ± 0.05	1.06 ± 0.08	O_4-H...O_5	~ 0	0.62 ± 0.04	0.96 ± 0.06	O_4-H...O_5	0.02 ± 0.01
O_7	-	0.10 ± 0.03	O_4-H...O_6	0.02 ± 0.01	-	0.16 ± 0.03	O_4-H...O_6	0.03 ± 0.01
O_8	0.71 ± 0.06	0.75 ± 0.07	O_6-H...O_4	0.05 ± 0.02	0.36 ± 0.03	0.55 ± 0.05	O_6-H...O_4	0.04 ± 0.01
O_9	0.61 ± 0.05	0.89 ± 0.06	O_6-H...O_5	~ 0	0.54 ± 0.04	0.62 ± 0.05	O_6-H...O_5	0.01 ± 0.01
O_{10}	-	0.36 ± 0.06	O_8-H...O_9	0.02 ± 0.01	-	0.22 ± 0.03	O_8-H...O_9	0.04 ± 0.02
O_{11}	0.43 ± 0.06	0.65 ± 0.07	O_8-H...O_{10}	0.04 ± 0.02	0.38 ± 0.04	0.60 ± 0.05	O_8-H...O_{10}	0.06 ± 0.01
Total	4.59 ± 0.06	7.00 ± 0.07	O_{11}-H...O_{10}	0.05 ± 0.02	3.92 ± 0.04	6.6 ± 0.04	O_{11}-H...O_{10}	0.03 ± 0.01
Total	11.59 ± 0.07			0.25 ± 0.02	10.52 ± 0.04			0.29 ± 0.01

Table S6: Average number hydrogen bonds (HB) per surfactant between the water molecules and the maltose headgroup and between selected atoms belonging to the surfactant head groups. The HB distance (O…O) = 3.5 Å and angle O-H…O is from 120° to 180° (Umemura, Yuguchi et al. 2005) [a]and partially those computed by ref. (Chong, Hashim et al. 2006).

Listing 1: CHARMM-compatible parameters for CH3-CH2-O-THP2. Parameters are compatible with the CHARMM hexopyranose monosaccharide force field described in ref. (Guvench, Greene *et al.* 2008). Complete CHARMM carbohydrate force field files, which also include hexopyranose monosaccharides, acyclic polyalcohols, acyclic carbohydrates, and inositol, can be downloaded from http://mackerell.umaryland.edu.

```
* Stream file with CH3-CH2-O-THP2
*

read rtf card append
* CH3-CH2-O-THP2
*
36 1

PRES POEA  0.20 ! prabhu, make model compound oetp by adding axial
dele atom H1A  ! O-ethyl to C1; apply to THP2
GROUP
ATOM C1 CC311D 0.29 !
ATOM H1B HCA1 0.09 !
ATOM OE OC301 -0.36 !
ATOM C6 CC321 0.00 !
ATOM H61 HCA2 0.09 !
ATOM H62 HCA2 0.09 !
ATOM C7 CC331 -0.27 !
ATOM H71 HCA3 0.09 !
ATOM H72 HCA3 0.09 !
ATOM H73 HCA3 0.09 !

BOND OE C1 OE C6 C6 C7
BOND C6 H61 C6 H62
BOND C7 H71 C7 H72 C7 H73
! I J K L R(IK) T(IKJ) PHI T(JKL) R(KL)
IC OE C1 O5 C5 0.0000 0.0000 70.41 0.0000 0.0000
IC O5 C1 OE C6 0.0000 0.0000 71.27 0.0000 0.0000
IC C1 OE C6 H61 0.0000 0.0000 47.22 0.0000 0.0000
IC C5 O5 C1 H1B 0.0000 0.0000 -168.02 0.0000 0.0000
IC H61 OE *C6 H62 0.0000 0.0000 -120.00 0.0000 0.0000
IC C1 OE C6 C7 0.0000 0.0000 180.00 0.0000 0.0000
IC OE C6 C7 H71 0.0000 0.0000 47.22 0.0000 0.0000
IC H71 C6 *C7 H72 0.0000 0.0000 120.00 0.0000 0.0000
IC H73 C6 *C7 H72 0.0000 0.0000 -120.00 0.0000 0.0000


PRES POEB  0.20 ! prabhu, make model compound oetp by adding equatorial
dele atom H1B  ! O-ethyl to C1; apply to THP2
GROUP
ATOM C1 CC311D 0.29 !
```

```
ATOM H1A HCA1 0.09 !
ATOM OE OC301 -0.36 !
ATOM C6 CC321 0.00 !
ATOM H61 HCA2 0.09 !
ATOM H62 HCA2 0.09 !
ATOM C7 CC331 -0.27 !
ATOM H71 HCA3 0.09 !
ATOM H72 HCA3 0.09 !
ATOM H73 HCA3 0.09 !

BOND OE C1 OE C6 C6 C7
BOND C6 H61 C6 H62
BOND C7 H71 C7 H72 C7 H73
! I J K L R(IK) T(IKJ) PHI T(JKL) R(KL)
IC OE C1 O5 C5 0.0000 0.0000 -175.00 0.0000 0.0000
IC O5 C1 OE C6 0.0000 0.0000 71.27 0.0000 0.0000
IC C1 OE C6 H61 0.0000 0.0000 47.22 0.0000 0.0000
IC C5 O5 C1 H1A 0.0000 0.0000 65.00 0.0000 0.0000
IC H61 OE *C6 H62 0.0000 0.0000 -120.00 0.0000 0.0000
IC C1 OE C6 C7 0.0000 0.0000 180.00 0.0000 0.0000
IC OE C6 C7 H71 0.0000 0.0000 47.22 0.0000 0.0000
IC H71 C6 *C7 H72 0.0000 0.0000 120.00 0.0000 0.0000
IC H73 C6 *C7 H72 0.0000 0.0000 -120.00 0.0000 0.0000

END

! added parameters
read para card append
* Parameters needed for OETP
*

ANGLES
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OC301 CC321 CC331 45.00 111.50 ! OC3C7M CC321 CC331 par_all35_carb.prm

DIHEDRALS
! atom types               Kchi  n delta
CC321 OC301 CC311D HCA1 0.284 3 0.0 ! CC331 OC301 CC311D HCA1
OC301 CC321 CC331 HCA3 0.20  3 0.0 ! OC301 CC321 CC3163 HCA1
CC311D OC301 CC321 HCA2 0.284 3 0.0 ! CC311D OC301 CC331 HCA3

CC321 OC301 CC311D OC3C61 0.36 1 180.0 ! prabhu, OETP QM phi-psi scan
CC321 OC301 CC311D OC3C61 0.52 2 0.0 ! " MCSA fit "
CC321 OC301 CC311D OC3C61 0.83 3 180.0 ! " MP2/cc-pVTZ//MP2/6-31G*

CC311D OC301 CC321 CC331 0.72  1 180.0 ! prabhu, OETP QM phi-psi scan
CC311D OC301 CC321 CC331 0.34  2 180.0 ! " MCSA fit "
CC311D OC301 CC321 CC331 0.12  3 180.0 ! " MP2/cc-pVTZ//MP2/6-31G*
```

CC321 OC301 CC311D CC321C 0.58 1 180.0 ! prabhu, OETP QM phi-psi scan
CC321 OC301 CC311D CC321C 0.69 2 180.0 ! " MCSA fit "
CC321 OC301 CC311D CC321C 1.16 3 0.0 ! " MP2/cc-pVTZ//MP2/6-31G*

END

References:

Chong, T. T., R. Hashim, et al. (2006). "Molecular Dynamics Simulation of Monoalkyl Glycoside Micelles in Aqueous Solution: Influence of Carbohydrate Headgroup Stereochemistry." J. Phys. Chem. B **110**(10): 4978-4984.

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Umemura, M., Y. Yuguchi, et al. (2005). "Hydration at glycosidic linkages of malto- and cello-oligosaccharides in aqueous solution from molecular dynamics simulation: Effect of conformational flexibility." Journal of Molecular Structure: THEOCHEM **730**(1-3): 1-8.