Supplementary Material (ESI) for PCCP
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Supplementary Material
Efficient solvent boundary potential for hybrid potential simulations

Alexey Aleksandrov & Martin Field*
Laboratoire de Dynamique Moléculaire,
Institut de Biologie Structurale Jean-Pierre Ebel (CEA, CNRS UMR5075, Université Joseph Fourier - Grenoble I),
41 rue Jules Horowitz, 38027 Grenoble, France.
*Email: martin.field@ibs.fr

Force field determination for acetyl-Coenzyme A and oxaloacetate

As part of this study, we report a force field model for acetyl-Coenzyme A (COA) and oxaloacetate (OAA). The force field was developed so as to be compatible with the CHARMM27 force field for proteins and nucleic acids [1, 2], and with the TIP3P water model [3].

Force field parameters were developed for the keto, enol and enolate forms of COA, and for the dianionic state of oxaloacetate that predominates at neutral pH. Structures were taken from the PDB. Atomic charges were derived from a supermolecule *ab initio* approach and Lennard-Jones parameters were adopted from the CHARMM27 force field [1, 2, 4]. We calculated the *ab initio* energies and geometries of a water molecule interacting with each compound at a few, selected positions. This supermolecule approach is known to give a good balance between solute–water and water–water interactions in the force field [1, 2]. Good agreement was obtained between the *ab initio* and force field data with a rms deviation for the energies of 0.3 kcal/mol. The model also reproduces well the conformational *ab initio* energies and geometries of the individual species, and the interactions between acetyl-CoA, oxaloacetate and protein.

Optimization of the intermolecular force field parameters

We adopted a force field of the CHARMM27 form [1] and used it to simulate complexes between acetyl-CoA, oxaloacetate and citrate synthase in aqueous solution. The intermolecular energy consists of Lennard-Jones and Coulomb terms. As in the development of the CHARMM27 force field, we employ supermolecule, quantum chemical

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calculations on complexes between a model compound and a single water molecule to parametrize the intermolecular force field terms. In these calculations, the internal geometries of the model compound and the water molecule are held fixed. The model compounds' geometries were determined by optimizing them at the HF/6-31G(d) level, whereas the water geometry was taken from the TIP3P model [3].

A few water positions were considered for each model compound. Each supermolecule structure was optimized at the HF/6-31G(d) level by varying the interaction distance and a single angle, to find the local minimum for the water position. From the resulting optimal structure, the interaction energy was calculated. No correction for basis set superposition error was made. The *ab initio* interaction energies were scaled by a factor of 1.16 and the *ab initio* interaction distances were reduced by 0.2 Å to compensate for overestimated interaction distances with the Hartree-Fock model (due to neglected electron correlation)[1].

The force field parameters to be optimized were adjusted to reproduce these "corrected" ab initio interaction energies and water positions. Initial partial charges were obtained from a Mulliken population analysis of the HF/6-31G(d) wavefunction and were compared with charges of similar molecules for which CHARMM parameters are known. Lennard-Jones parameters were adapted from the CHARMM27 force field for similar chemical groups.

For acetyl-Coa and OAA, we parametrized 3 model compounds: oxaloacetate, methylphosphate, and different tautomeric forms of ethyl thioacetate: keto, enolate, and enol. We optimized the interaction distance and the (corrected) *ab initio* data were then fitted by varying manually the model compound charges. This involved reoptimizing the compound-water distance after each parameter change. In addition to the water-compound interactions, the *ab intio* dipole moments were also used as target data in the partial charge optimization.

We first consider the supermolecule calculations for model compounds interacting with individual water molecules. Detailed results are given in Tables 3–7 for the five species that were considered. The first corresponds to oxaloacetate; the second, third, and fourth correspond to the thioacetate of acetyl-CoA and the last compound corresponds to the phosphate group of acetyl-CoA. Overall, very good agreement was obtained between the *ab initio* and force field data. The rms deviation for the energies was 0.3 kcal/mol, averaged over all fragments, all water positions, and all water orientations. To obtain this agreement, only small adjustments were required to the starting values that were chosen for the atomic charges.

The dipole moments of the compounds are presented in Table 8. It can be seen

that the force field values are systematically larger than the gas phase QC values, which is desirable due to the omission of explicit electronic polarizability from the force field [4]. Angles between the empirical and QC dipole moments are also given in Table 8, showing that they are almost collinear.

Optimization of the intramolecular force field parameters

In a force field treatment, the intramolecular geometry is mainly determined by the minimum energy values of the bond length and bond angle terms, and by the phase and multiplicity of the dihedrals. Initial values for the minimum energy bond lengths, bond angles and torsion angles were taken directly from the *ab initio* structures that were obtained by geometry optimizations at the HF/6-31G(d) level. Starting guesses for the bond and angle force constants, and for the dihedral force constants and phases were taken from the CHARMM27 force field [1] for related, small molecular fragments. The geometrical and dihedral parameters were then optimized by fitting to the *ab initio* structures. At each parameter optimization step, the structure was minimized with the force field model, using a Powell conjugate gradient algorithm and stopping when the rms energy gradient reached 10^{-6} kcal/mol/Å. The quality of the parameters was assessed by the rms coordinate deviation between the force field and *ab initio* structures, and the similarities of the *ab initio* and force field torsional energy profiles (see below). The bond and angle geometries, and the dihedral geometries were then updated manually and a new round of optimization was performed. This procedure was repeated until a satisfactory agreement was achieved, namely a coordinate rms deviation of less than 0.1 Å and energy differences of at most 0.5 kcal/mol.

To characterize molecular flexibility, we examined large, lower-frequency fluctuations, which involve the soft dihedral angles. Fig. 1–3 illustrate the softer dihedral fluctuations in oxaloacetate and acetyl-CoA. For OAA, energy profiles are shown for the dihedral angle that links the carboxyl group to the rest of the molecule, whereas for acetyl-CoA, energy profiles are shown for the dihedral angles that link the acetyl-pantetheine and thioacetic groups (Fig. 2 and 3, respectively). Again, agreement is very good between the force field and the *ab initio* profiles, not only for the energy wells, but also for the barriers between wells. These softer, dihedral degrees of freedom are very important for accurately describing the conformational free energy surfaces of the molecules.

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Acetyl-CoA, OAA, and citrate synthase interactions: molecular dynamics simulations

We performed MD simulations of the acetyl-CoA:CS complex for 2 nanoseconds. The protein:acetyl-CoA complex was solvated by a 24 Å water sphere centered on the oxaloacetate binding site whereas the more distant regions were modeled as a dielectric continuum (see Methods).

We computed rms deviations from the crystal structure, averaging over the last 1 ns of the 2 ns simulations (Table 1). By superimposing the oxaloacetate on the crystal structure, we obtained intramolecular OAA deformations of less than 0.30 Å. The equivalent value for acetyl-CoA was 0.47 Å. Superimposing the protein backbone on the crystal structure, we obtained rms deviations of 0.49, 0.69 and 0.56 Å for OAA, COA and the protein backbone, respectively. Figure 4 shows the good structural agreement between the MD simulation of acetyl-CoA:CS and the experimental X-ray structure [5] (PDB entry code 4CSC). The interactions between OAA, acetyl-CoA and the protein are also well-reproduced (Tables 2).

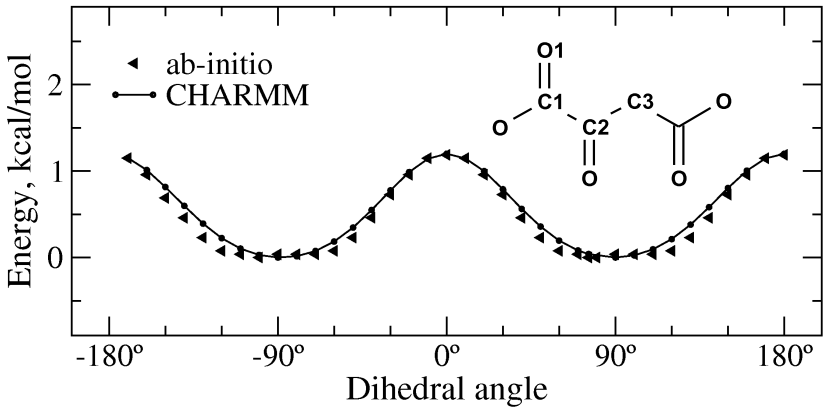

Figure 1: Comparing *ab initio* and force field energies for the dihedral angle of oxaloacetate. The dihedral angle is defined by the atoms labelled (C3-C2-C1-O1). The solid line corresponds to force field energies.

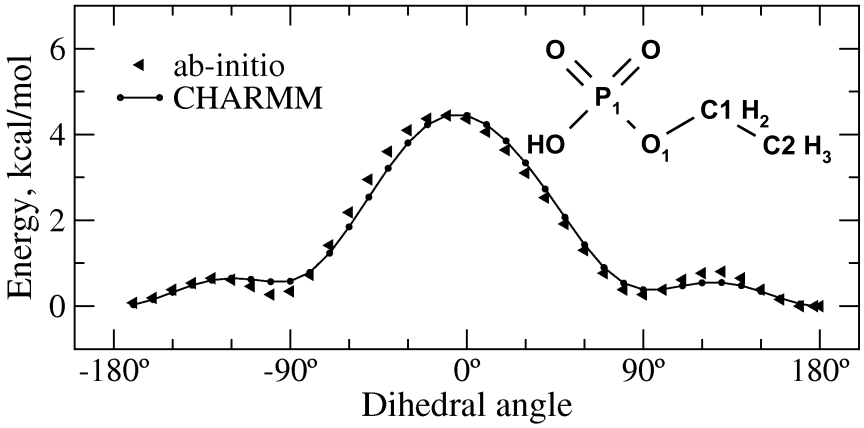

Figure 2: Comparing *ab initio* and force field energies for the dihedral angle of ethylphosphate. The dihedral angle is defined by the atoms labelled (C2-C1-O1-P1). The solid line corresponds to force field energies.

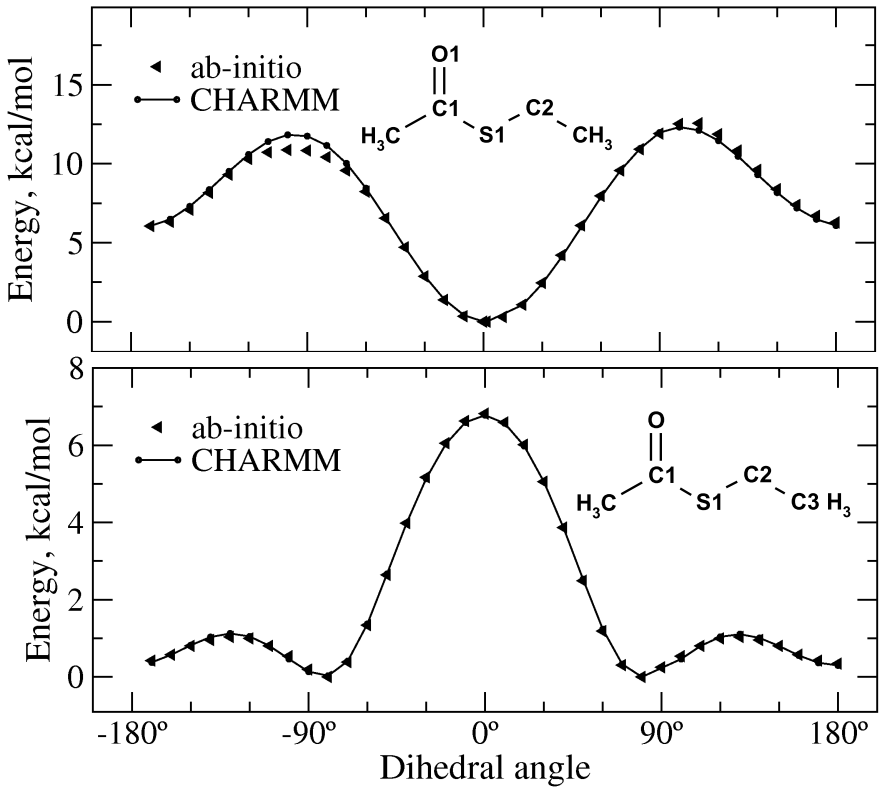

Figure 3: Comparing *ab initio* and force field energies for two dihedral angles that link the acetyl group. The dihedral angles are defined by the atoms labelled in each inset (C2-S1-C1-O1 and C3-C2-S1-C1). In each panel, the solid line corresponds to force field energies.

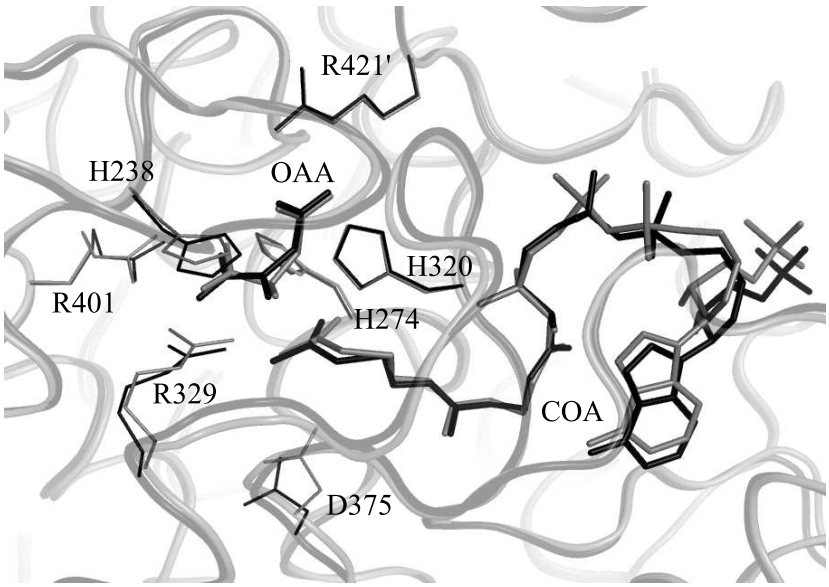

Figure 4: View of the acetyl-coenzyme A binding site from the final nanosecond of the MD trajectory and the experimental X-ray structure (PDB entry 4CSC). COA and OAA are in stick representation, important residues are shown as lines, the experimental structure is gray, and the MD structure is black.

Table 1: Rms deviations (Å) for the acetyl-CoA:CS complex

atoms	RMSD
OAA[a]	0.29
OAA[b]/backbone	0.49
COA[a]	0.47
COA[b]/backbone	0.69
backbone	0.56

Rms deviations between the MD and crystal structures. [a]After superimposing the MD ligand on the ligand in the crystal structure. [b]After superimposing the protein backbone on the crystal structure. Non-hydrogen atoms only in each case.

Table 2: Selected distances (Å) between atoms of acetyl-CoA, OAA, and citrate-synthase

atom pair	MD simulation	[a]Xray structure
$NH2_{R401}$ $O1A_{OAA}$	2.8	2.8
$NH1_{R401}$ $O1B_{OAA}$	2.7	2.8
$N\epsilon_{R421}$ $O4A_{OAA}$	2.8	2.7
$NH2_{R421}$ $O4B_{OAA}$	2.7	2.8
$N\delta1_{H238}$ $O4B_{OAA}$	2.7	2.8
$N\delta1_{H274}$ O_{COA}	3.0	2.9
O_{L273} $N4P_{COA}$	3.1	2.9
N_{G317} $O5P_{COA}$	2.9	2.8
O_{Y318} $N8P_{COA}$	3.1	3.0

All atoms (left) are labelled by the amino acid to which they belong. [a]PDB entry 4CSC.

Table 3: Interactions between a probe water and selected oxaloacetate sites

	ab initio/force field results		
probe site	energy (kcal/mol)	distance (Å)	angle (°)
O2C2	-14.04/-14.27	1.80/1.72	0.0
O2C2	-13.16/-13.17	1.80/1.73	60.0
O2C2	-12.09/-11.60	1.80/1.74	120.0
O2C2	-11.78/-10.99	1.80/1.74	180.0
O2C2	-11.90/-11.39	1.80/1.74	240.0
O2C2	-13.09/-13.09	1.80/1.73	300.0

Table 4: Interactions between a probe water and selected sites of the keto form of ethyl thioacetate

	ab initio/force field results		
probe site	energy (kcal/mol)	distance (Å)	angle (°)
OC	-4.21/-4.43	1.81/1.83	0.0
OC	-4.29/-4.41	1.81/1.83	60.0
OC	-4.60/-4.46	1.81/1.83	120.0
OC	-4.74/-4.49	1.81/1.83	180.0
OC	-4.69/-4.50	1.81/1.83	240.0
OC	-4.47/-4.47	1.81/1.83	300.0

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Table 5: Interactions between a probe water and selected sites of the enolate form of ethyl thioacetate

	ab initio/force field results		
probe site	energy (kcal/mol)	distance (Å)	angle (°)
OC	-12.43/-12.54	1.90/1.77	0.0
OC	-12.36/-12.44	1.90/1.77	60.0
OC	-12.47/-12.41	1.90/1.77	120.0
OC	-12.51/-12.51	1.90/1.77	180.0
OC	-12.51/-12.51	1.90/1.77	240.0
OC	-12.47/-12.47	1.90/1.77	300.0
CH3C	-8.64/-7.76	2.26/2.07	0.0
CH3C	-11.59/-12.38	2.22/1.99	180.0

Table 6: Interactions between a probe water and selected sites of the enol form of methyl thioacetate

	ab initio/force field results		
probe site	energy (kcal/mol)	distance (Å)	angle (°)
HO	-7.27/-6.86	1.73/1.83	0.0
HO	-6.87/-6.87	1.74/1.83	60.0
HO	-6.29/-6.77	1.77/1.83	120.0
H21CH3	-1.63/-1.72	3.02/2.76	0.0
H21CH3	-2.16/-1.83	2.89/2.74	60.0
H21CH3	-2.12/-1.87	2.93/2.73	120.0
H11CH3	-0.78/-0.78	2.66/2.58	0.0
H11CH3	-0.74/-0.77	2.67/2.59	60.0
H11CH3	-0.65/-0.71	2.69/2.59	120.0
OC	-4.07/-4.06	1.93/1.91	0.0
OC	-4.43/-4.51	1.91/1.90	60.0
OC	-4.43/-4.95	1.91/1.88	120.0
OC	-4.34/-4.70	1.92/1.89	180.0
OC	-4.07/-4.22	1.93/1.90	240.0
OC	-4.16/-4.08	1.91/1.91	300.0

Table 7: Interactions between a probe water and selected monoanionic methylphosphate sites

	ab initio/force field results		
probe site	energy (kcal/mol)	distance (Å)	angle (°)
O2C2	-7.68/-8.34	1.80/1.77	0.0
O2C2	-7.30/-7.56	1.80/1.78	60.0
O2C2	-6.88/-6.87	1.80/1.79	120.0
O2C2	-6.96/-6.96	1.80/1.79	180.0
O2C2	-7.46/-7.49	1.80/1.78	240.0
O2C2	-7.76/-8.27	1.80/1.77	300.0

Table 8: *Ab initio* and force field dipole moments

compound	dipole moment (debye)		angle
	abinitio	force field	(°)
oxaloacetate	1.67	2.04	3.1
keto ethyl thioacetate	1.16	1.70	16.3
enolate ethyl thioacetate	4.74	6.35	11.7
enol methyl thioacetate	2.25	1.69	8.7
monoanionic methylphosphate	6.58	8.96	1.1

Force field for acetyl-CoA and oxaloacetate

The force field is presented below in the format appropriate for the CHARMM simulation program [6]. Atom types, atom charges, and chemical bonding information are contained in a "topology file". Bond lengths and force constants, bond angle values and associated force constants, dihedral parameters and van der Waals parameters are contained in a "parameter file".

References

[1] Mackerell, A. et al. (1998) An all-atom empirical potential for molecular modelling and dynamics study of proteins. *J. Phys. Chem. B 102*, 3586–3616.

[2] Mackerell, A., Wiorkiewicz-Kuczera, J., and Karplus, M. (1995) An all-atom empirical energy force-field for the study of nucleic acids. *J. Am. Chem. Soc. 117*, 11946–11975.

[3] Jorgensen, W., Chandrasekar, J., Madura, J., Impey, R., and Klein, M. (1983) Comparison of simple potential functions for simulating liquid water. *J. Chem. Phys. 79*, 926–935.

[4] Foloppe, N., and MacKerell, A. (2000) All–atom empirical force field for nucleic acids: I. Parameter optimization based on small molecule and condensed phase macromolecular target data. *J. Comp. Chem. 21*, 86–104.

[5] Karpusas, M., Holland, D., and Remington, S. (1991) 1.9-A structures of ternary complexes of citrate synthase with D- and L-malate: mechanistic implications. *Biochemistry 30*, 6024–31.

[6] Brooks, B. R. et al. (2009) CHARMM: the biomolecular simulation program. *J. Comp. Chem. 30*, 1545–1614.

Topology file: top_coa.inp

```
* CHARMM topology for acetyl-CoA and oxaloacetate
* Alexey Aleksandrov and Martin Field 10/2009
* Alexey.Aleksandrov at polytechnique.edu
27  1
```

```
RESI COA         -3.00  ! acetyl-CoA, keto form
GROUP
ATOM CH3  CT3    -0.27
ATOM H11  HA      0.09
ATOM H21  HA      0.09  !     O         H12
ATOM H31  HA      0.09  !      \\       |
ATOM C    C       0.44  !       C--S1P--C2P--
ATOM O    O      -0.39  !      /         |
ATOM S1P  S      -0.09  ! H11-CH3       H22
ATOM C2P  CT2    -0.14  !     | \
ATOM H12  HA      0.09  !   H21  H31
ATOM H22  HA      0.09

GROUP
ATOM C3P  CT2    -0.02
ATOM H13  HA      0.09  !   H13       O5P  H16
ATOM H23  HA      0.09  !   |         ||   |
ATOM N4P  NH1    -0.47  ! --C3P--N4P--C5P--C6P--
ATOM H4P  H       0.31  !   |    |         |
GROUP                   !   H23  H4P       H26
ATOM C5P  C       0.51
ATOM O5P  O      -0.51
GROUP
ATOM C6P  CT2    -0.18
ATOM H16  HA      0.09
ATOM H26  HA      0.09

GROUP
ATOM C7P  CT2    -0.02
ATOM H17  HA      0.09  !   H17       O9P
ATOM H27  HA      0.09  !   |         ||
ATOM N8P  NH1    -0.47  ! --C7P--N8P--C9P--
ATOM H8P  H       0.31  !   |    |
GROUP                   !   H27  H8P
ATOM C9P  C       0.51
```

```
ATOM O9P  O      -0.51

GROUP
ATOM CAP  CT1     0.14
ATOM OAP  OH1    -0.66  !   HAP  CDP(H3)
ATOM HO2  H       0.43  !   |    |
ATOM HAP  HA      0.09  ! --CAP--CBP--
GROUP                   !   |    |
ATOM CBP  CT1     0.00  !   OAP  CEP(H3)
GROUP                   !   |
ATOM CEP  CT3    -0.27  !   HO2
ATOM H1EP HA      0.09
ATOM H2EP HA      0.09
ATOM H3EP HA      0.09
GROUP
ATOM CDP  CT3    -0.27
ATOM H1DP HA      0.09
ATOM H2DP HA      0.09
ATOM H3DP HA      0.09

GROUP
ATOM CCP  CN9    -0.08
ATOM H1CP HN9     0.09  !   H1CP      O1P2
ATOM H2CP HN9     0.09  !   |         |
ATOM O6A  ON2    -0.62  ! --CCP--O6A--P2--O12--
ATOM P2   P       1.46  !   |         |
ATOM O1P2 ON3    -0.83  !   H2CP      O2P2
ATOM O2P2 ON3    -0.83
ATOM O12  ON2    -0.63

GROUP
ATOM P    P       1.50  ! ADE
ATOM O1P  ON3    -0.82  !             H61  H62!
ATOM O2P  ON3    -0.82  !               \  /
ATOM O5'  ON2    -0.61  !                N6
ATOM C5'  CN8B   -0.08  !                |
```

```
ATOM H5'  HN8     0.09  !                C6
ATOM H5'' HN8     0.09  !              //  \
GROUP                   !              N1   C5--N7\\
ATOM C4'  CN7     0.16  !              |    ||     C8-H8
ATOM H4'  HN7     0.09  !              C2   C4--N9/
ATOM O4'  ON6B   -0.50  !             / \\ /     \
ATOM C1'  CN7B    0.16  !           H2   N3       \
ATOM H1'  HN7     0.09  !                          \
GROUP                   !                           \
ATOM N9   NN2    -0.05  !                            \
ATOM C5   CN5     0.28  !        O1P    H5' H4'  O4'  \
ATOM N7   NN4    -0.71  !         |      |    \ /   \  \
ATOM C8   CN4     0.34  !        -P-O5'-C5'---C4'    C1'
ATOM H8   HN3     0.12  !         |      |     \     / \
ATOM N1   NN3A   -0.74  !        O2P    H5''   C3'--C2' H1'
ATOM C2   CN4     0.50  !                     / \   / \
ATOM H2   HN3     0.13  !                  O3' H3' O2' H2''
ATOM N3   NN3A   -0.75  !                   |       |
ATOM C4   CN5     0.43  !                         H2'
ATOM C6   CN2     0.46
ATOM N6   NN1    -0.77
ATOM H61  HN1     0.38
ATOM H62  HN1     0.38
GROUP
ATOM C2'  CN7B    0.14
ATOM H2'' HN7     0.09
ATOM O2'  ON5    -0.66
ATOM H2'  HN5     0.43

GROUP                   ! 3'terminal phosphate
ATOM C3'  CN7     0.01  !       /
ATOM H3'  HN7     0.09  !      O3'
ATOM P3   P       1.50  !      |
ATOM O1P3 ON3    -0.82  ! O1P3=P3=O2P3
ATOM O2P3 ON3    -0.82  !      |
ATOM O3'  ON2    -0.62  !      O3T-H3T
```

```
ATOM O3T  ON4    -0.68  !
ATOM H3T  HN4     0.34

BOND   CH3  H11  CH3  H21  CH3  H31
BOND   CH3    C    C    O  S1P    C
BOND   C2P  S1P  C2P  H12  C2P  H22
BOND   C2P  C3P
BOND   C3P  H13  C3P  H23  C3P  N4P
BOND   N4P  H4P  N4P  C5P
BOND   C5P  O5P  C5P  C6P
BOND   C6P  H16  C6P  H26
BOND   C6P  C7P
BOND   C7P  H17  C7P  H27  C7P  N8P
BOND   N8P  H8P  N8P  C9P
BOND   C9P  O9P
BOND   C9P  CAP
BOND   CAP  OAP  CAP  HAP  CAP  CBP  OAP  HO2
BOND   CBP  CDP  CBP  CEP
BOND   CDP  H1DP CDP  H2DP CDP  H3DP
BOND   CEP  H1EP CEP  H2EP CEP  H3EP
BOND   CBP  CCP
BOND     P  O12  O12  P2
BOND    P2  O1P2 P2   O2P2 P2   O6A
BOND   O6A  CCP  CCP  H1CP CCP  H2CP

! ADE
BOND P    O1P   P    O2P   P    O5'
BOND O5'  C5'   C5'  C4'   C4'  O4'   C4'  C3'   O4'  C1'
BOND C1'  N9    C1'  C2'   N9   C4    N9   C8    C4   N3
BOND C2   N1    C6   N6
BOND N6   H61   N6   H62   C6   C5    C5   N7
BOND C2'  C3'   C2'  O2'   O2'  H2'   C3'  O3'
BOND C1'  H1'   C2'  H2''  C3'  H3'   C4'  H4'   C5'  H5'
BOND C5'  H5''  C8   H8    C2   H2
DOUBLE  N1  C6  C2   N3    C4   C5    N7   C8
```

```
! 3PHO
BOND O3'  P3     P3  O1P3   P3  O2P3   P3  O3T  O3T  H3T

IMPR  C    S1P  CH3  O
IMPR  N4P  C5P  C3P  H4P
IMPR  C5P  C6P  N4P  O5P
IMPR  N8P  C9P  C7P  H8P
IMPR  C9P  CAP  N8P  O9P
IMPR  N6   C6   H61  H62
IMPR  C6   N1   C5   N6


PRES ELT         -1.00 ! convert keto form of acetyl-CoA into enolate
GROUP
ATOM   CH3  CE2  -0.83
ATOM   H11  HE2   0.09
ATOM   H21  HE2   0.09
ATOM     C    C   0.30
ATOM     O    O  -0.60
ATOM   S1P    S  -0.09
ATOM   C2P  CT2  -0.14
ATOM   H12   HA   0.09
ATOM   H22   HA   0.09
DELE  ATOM  H31


PRES ETE          0.00 ! converts keto form of acetyl-CoA into enol
GROUP
ATOM CH3  CE2    -0.55
ATOM H11  HE2     0.22
ATOM H21  HE2     0.22 !  H--O         H12  H13
ATOM C    C       0.28 !      \\       |    |
ATOM O    OH1    -0.53 !       C--S1P--C2P--C3P-H23
ATOM H    H       0.41 !      /        |    |
ATOM S1P  S      -0.09 ! H11-CH3       H22  H33
ATOM C2P  CT2    -0.14 !     |
```

```
ATOM H12  HA      0.09 !     H21
ATOM H22  HA      0.09 !
DELE  ATOM  H31
BOND H  O


RESI OAA        -2.00 ! oxaloacetate
GROUP
ATOM  C4  CC     0.62 !  O1A       H3A     O4A(-)
ATOM  O4A OC    -0.76 !    \\       |     /
ATOM  O4B OC    -0.76 !     C1--C2--C3--C4
ATOM  C3  CT2   -0.28 !    /    ||  |    \\
ATOM  H3A HA     0.09 ! O1B(-)  O2 H3B     O4B
ATOM  H3B HA     0.09 !
GROUP
ATOM  C2  CC     0.45
ATOM  O2  O     -0.55
ATOM  C1  CC     0.62
ATOM  O1A OC    -0.76
ATOM  O1B OC    -0.76
BOND    C4  O4A   C4  O4B   C4   C3
BOND    C3  H3A   C3  H3B   C3   C2
BOND    C2   O2   C2   C1
BOND    C1  O1A   C1  O1B
IMPR C1 C2 O1A O1B
IMPR C4 C3 O4A O4B
IMPR C2 C3 C1  O2


END
```

Parameter file: par_coa.prm

```
* CHARMM parameter file for acetyl-CoA and oxaloacetate
* Alexey Aleksandrov and Martin Field 10/2009
* Alexey.Aleksandrov at polytechnique.edu
```

```
BONDS
S       C       198.00  1.8180
CT1     CN9     222.50  1.5380
C       CE2     250.00  1.3550
C       OH1     230.00  1.4000
CC      CC      493.60  1.5070
CC      CD      493.60  1.5070

ANGLES
CT2     S       C         34.00   95.00
S       C       O         80.00  121.00
S       C       CT3       50.00  114.00
C       CT1     OH1       50.00  110.50
CN9     CT1     CT1       53.35  111.00    8.00   2.5610
CT3     CT1     CN9       53.35  114.00    8.00   2.5610
CT1     CN9     HN9       33.43  110.10   22.53   2.1790
CT1     CN9     ON2       45.00  111.50
C       CE2     HE2       55.50  120.50
O       C       CE2       80.00  133.50
S       C       CE2       50.00  114.00
S       C       OH1       58.00  116.20
C       OH1     H         65.00  108.00
OH1     C       CE2       45.20  120.00
CC      CT2     CC        69.10  120.60
CT2     CC      CC        57.80  113.40
CC      CC      OC        47.40  116.60
O       CC      CC        84.30  117.00
CC      CD      OH1       47.40  116.60
CC      CD      OB        47.40  116.60
O       CC      CD        84.30  117.00
CT2     CC      CD        57.80  113.40

DIHEDRALS
C       S       CT2     HA      0.0   3    0.0
HA      CT3     C       S       0.04  3    0.0
```

C	S	CT2	CT2	0.24	1	180.0
C	S	CT2	CT2	0.37	3	0.0
C	S	CT2	CT3	0.24	1	180.0
C	S	CT2	CT3	0.37	3	0.0
O	C	S	CT2	3.73	1	180.0
O	C	S	CT2	2.07	2	180.0
CT3	C	S	CT2	2.63	1	180.0
CT3	C	S	CT2	2.56	2	180.0
NH1	C	CT2	CT2	2.98	1	0.0
CT2	CT2	NH1	C	1.44	1	180.0
CT2	CT2	NH1	C	0.30	3	180.0
NH1	C	CT1	OH1	0.00	3	0.0
O	C	CT1	OH1	0.00	3	0.0
NH1	C	CT1	HA	0.00	3	0.0
O	C	CT1	HA	0.00	3	0.0
CT1	CT1	CN9	HN9	0.04	3	0.0
CT3	CT1	CN9	HN9	0.04	3	0.0
CT3	CT1	CN9	ON2	0.19	3	0.0
CT1	CT1	CN9	ON2	0.16	1	180.0
CT1	CT1	CN9	ON2	0.39	2	0.0
P	ON2	CN9	CT1	1.55	1	0.0
P	ON2	CN9	CT1	0.55	2	0.0
P	ON2	CN9	CT1	0.20	3	0.0
HE2	CE2	C	S	5.20	2	180.0
HE2	CE2	C	O	5.20	2	180.0
HE2	CE2	C	OH1	5.20	2	180.0
CE2	C	S	CT2	2.46	1	180.0
CE2	C	S	CT2	1.43	2	180.0
CE2	C	S	CT2	0.42	3	180.0
OH1	C	S	CT2	1.77	1	180.0
OH1	C	S	CT2	0.73	3	0.0
H	OH1	C	S	0.02	1	0.0
H	OH1	C	S	0.31	2	180.0
H	OH1	C	CE2	0.57	1	180.0
H	OH1	C	CE2	0.85	2	180.0
OC	CC	CC	CT2	0.20	2	180.0

```
OC      CC      CC      O       0.00  2  180.0
OB      CD      CC      CT2     0.20  2  180.0
OH1     CD      CC      CT2     0.20  2  180.0
OH1     CD      CC      O       0.00  2  180.0
OB      CD      CC      O       0.00  2  180.0

IMPROPER
C       S       CE2     OH1   120.00  0    0.0
CC      CT2     CC      O      50.00  0    0.0
CD      CC      OB      OH1    50.00  0    0.0
CC      CT2     CD      O      50.00  0    0.0
```