

Supporting Information

**Configuration Determination by Residual Dipolar Couplings:
Accessing the Full Conformational Space by Molecular Dynamics
with Tensorial Constraints**

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Table of Contents

General information to the MD runs with Orientational Constraints (MDOC)	4
Graphical representation of the tanh (x)	5
Norcamphor	6
Experimental data for norcamphor (1)	6
Coordinates of norcamphor in pdb-file format for the correct configuration	7
Coordinates of norcamphor in coo-file format for the correct configuration	9
Data file for COSMOS MD simulation (.cod) for norcamphor (1)	11
Data file for MSpin SVD fitting calculation for norcamphor	13
MDOC run Project file (.cos) for norcamphor	14
Command to start the MD simulation using the COSMOS backend	20
Synthetic spiroindene derivative	21
Experimental data ($^1D_{CH}$) for synthetic spiroindene derivative 2	21
Coordinates files of the spiroindene	22
Coordinates of spiroindene in pdb-file format (wrong configuration)	22
Coordinates of spiroindene in pdb-file format (correct configuration)	23
Coordinates of spiroindene in coo-file format (wrong configuration)	26
Coordinates of spiroindene in coo-file format (correct configuration)	29
Data file for COSMOS MD simulation (.cod) for spiroindene (2)	32
Staurosporine	34
Experimental data for staurosporine	34
Coordinates of staurosporine (3) in pdb file format	35
Coordinates of staurosporine in coo-file format (correct configuration)	38
Data file for MD simulation in program COSMOS for staurosporine 3	41
Oidiolactone B	43
Assignment data of Oidiolactone B	43
Experimental data for Oidiolactone B in PAN/DMSO- d_6	45
Coordinates of Oidiolactone B in pdb file format	46
Coordinates of Oidiolactone B in coo-file format	49
Data file for COSMOS MD simulation (.cod) for oidiolactone B (4)	51
References	53

General information to the MD runs with Orientational Constraints (MDOC)

The molecular dynamics simulations are performed on demonstrative examples of four small molecules with various degrees of flexibility starting from a rigid towards a flexible natural product. The molecules are the following: norcamphor **1**, synthetic spiroindene derivative **2**, a staurosporine **3** and Oidiolactone **4**.

As the above molecules are used for a principle demonstration set for the capabilities and application of the MDOC their constitution, configuration and the NMR assignment for each molecule was known in advance. For the application the MDOC simulations we have used only one bond C-H residual dipolar couplings ($^1D_{C-H}$ RDCs). For each MDOC run a coordinate file with the molecular geometry, a data file and a project file are necessary to be prepared for each single molecular model. In the following pages are given the experimental values of the used $^1D_{C-H}$ RDCs as orientational constraints, the coordinate file at least for the correct molecular structure, the data file and example project file together with an example command line for starting the MDOC simulation.

Graphical representation of the $\tanh(x)$

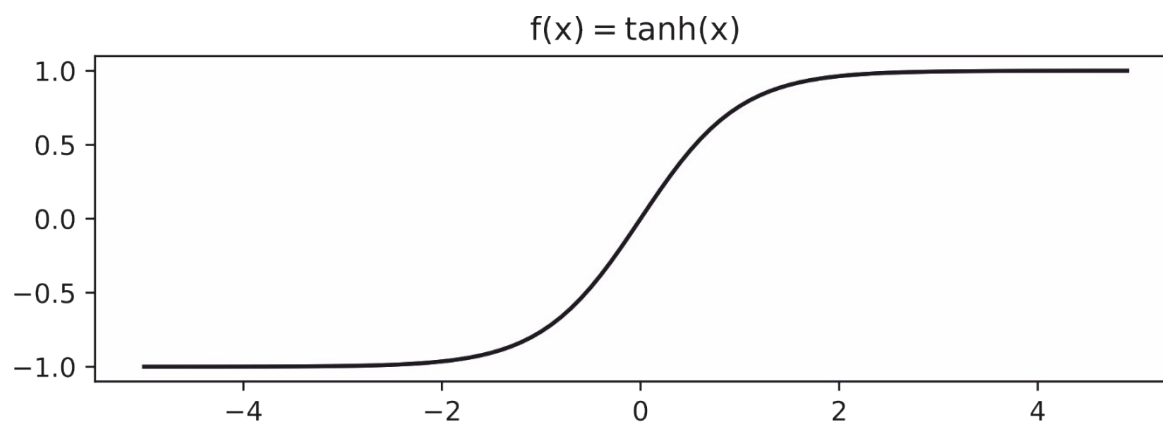


Figure S1. Graphical representation of the tangent hyperbolic function which represents the potential for the pseudo forces.

Norcamphor

Experimental data for norcamphor (1)

Table S1. Experimental data for norcamphor from 0.5 M solution in PEOMMA/TFE-d₂ with quadrupolar splitting of 7.6 Hz. Data is obtained from [1]

	$\delta_{1H}/[\text{ppm}]$	$\delta_{13C}/[\text{ppm}]$	$^1T_{CH}/[\text{Hz}]$	$^1D_{CH}/[\text{Hz}]$	Error [Hz]
C1-H1	2.08	49.4	151.8	1.4	0.5
C3-H3 exo	1.57	44.0	133.5	6.0	0.7
C3-H3 endo	1.33	44.0	139.1	5.0	0.7
C4-H4	2.16	34.5	143.5	-2.9	0.4
C5-H5 exo	1.31	25.6	124.8	-10.5	0.5
C5-H5 endo	0.94	25.6	138.9	5.3	0.5
C6-H6 exo	1.38	22.9	135.9	-1.9	0.6
C6-H6 endo	0.95	22.9	136.0	1.5	0.2
C7-H7 syn	1.27	36.5	139.8	5.8	0.2
C7-H7 anti	1.05	36.5	131.0	-7.1	0.2

Coordinates of norcamphor in pdb-file format for the correct configuration

The coordinates of norcamphor in a pdb-file format generated as an output from the program COSMOS with the correct configuration is given below. This configuration is marked as *Ref* throughout the manuscript.

```
HEADER      NO HEADER DEFINED AND DEFAULT DATE USED          01-JAN-00
AUTHOR      PDB FILE FORMAT GENERATED BY COSMOS
CRYST1      1.000      1.000      1.000      90.000      90.000      90.000 P1
COMPND
REMARK      CREATED FILE CONTAINS ONLY BASIC MOLECULAR DATA
REMARK CELL 1.0000 1.0000 1.0000 90.000 90.000 90.000 0.0000 0.0000 0.0000
REMARK SPGROUP P1
REMARK OPERATION CFF geometry optimization
REMARK ENERGY 273.439
REMARK FORCE_FIELD_ENERGIES BondEn=20.8036 AngleEn=126.713 TorsionEn=128.876
PiTorsionEn=2.40189 CoulombEn=-31.0965 VdWEn=25.7413
REMARK BPT_PSEUDO_ENERGIES IsotropicPsEn=0 TensorialPsEn=0 OrientationalPsEn=0.544335
REMARK NMR_PSEUDO_ENERGIES DistPsEn=0 RDCDistPsEn=0 RDCOrientPsEn=0 JCoupsPsEn=0
HETATM      1  O   UNK  0   1      0.641 -2.495 -1.754 1.00 0.00      O
HETATM      2  C4  NOP  A   1      0.692  0.211  0.458 1.00 0.00      C
HETATM      3  C6  NOP  A   1     -1.027  0.677 -1.146 1.00 0.00      C
HETATM      4  C2  NOP  A   1      0.476 -1.429 -1.109 1.00 0.00      C
HETATM      5  C1  NOP  A   1     -0.843 -0.822 -0.785 1.00 0.00      C
HETATM      6  C7  NOP  A   1     -0.554 -0.678  0.717 1.00 0.00      C
HETATM      7  C5  NOP  A   1      0.123  1.357 -0.411 1.00 0.00      C
HETATM      8  C3  NOP  A   1      1.588 -0.710 -0.402 1.00 0.00      C
HETATM      9  H1  C1   A   1     -1.702 -1.413 -1.111 1.00 0.00      H
HETATM     10  H3n C3   A   1      2.277 -0.174 -1.059 1.00 0.00      H
HETATM     11  H3x C3   A   1      2.150 -1.380  0.254 1.00 0.00      H
HETATM     12  H4  C4   A   1      1.227  0.599  1.328 1.00 0.00      H
HETATM     13  H5x C5   A   1     -0.258  2.195  0.179 1.00 0.00      H
HETATM     14  H5n C5   A   1      0.887  1.734 -1.095 1.00 0.00      H
HETATM     15  H6n C6   A   1     -1.093  0.949 -2.203 1.00 0.00      H
HETATM     16  H6x C6   A   1     -1.957  0.984 -0.660 1.00 0.00      H
HETATM     17  H7a C7   A   1     -1.346 -0.166  1.269 1.00 0.00      H
HETATM     18  H7s C7   A   1     -0.330 -1.630  1.205 1.00 0.00      H
CONNECT      1      4
CONNECT      2      8      6      7     12
CONNECT      3      7     15      5     16
CONNECT      4      1      5      8
CONNECT      5      6      3      4      9
CONNECT      6     18      5      2     17
CONNECT      7      3     13      2     14
CONNECT      8     11      4      2     10
CONNECT      9      5
CONNECT     10      8
CONNECT     11      8
CONNECT     12      2
CONNECT     13      7
CONNECT     14      7
```

CONECT	15	3							
CONECT	16	3							
CONECT	17	6							
CONECT	18	6							
MASTER		0	0	0	0	0	0	0	0

END

Coordinates of norcamphor in coo-file format for the correct configuration

The coordinates of norcamphor in a coo-file format generated for the program COSMOS with the correct configuration is given below. This configuration is marked as *Ref* throughout the manuscript.

```
$COO006
CELL 1.0000 1.0000 1.0000 90.000 90.000 90.000 0.0000 0.0000 0.0000
NAME
SPGROUP P1
OPERATION CFF geometry optimization
ENERGY 273.439
FORCE_FIELD_ENERGIES BondEn=20.8036 AngleEn=126.713 TorsionEn=128.876
PiTorsionEn=2.40189 CoulombEn=-31.0965 VdWEn=25.7413
BPT_PSEUDO_ENERGIES IsotropicPsEn=0 TensorialPsEn=0 OrientationalPsEn=0.544335
NMR_PSEUDO_ENERGIES DistPsEn=0 RDCDistPsEn=0 RDCOrientPsEn=0 JCoupPsEn=0
GROUP_TEXT 1 all Carbons
GROUP_TEXT 2 all Protons
GROUP_TEXT 3 DD tensor (constraints)
GROUP_TEXT 4 RDC values
GROUP_TEXT 5 Atoms for fixed distances
GROUP_TEXT 6 13C for RDC calc
GROUP_TEXT 7 tors angles
ATOMS 18
C3 6 1.58809 -0.71014 -0.40197 cmb -0.51130 1 0 8 5 7 16 0 0 0 0
C5 6 0.12278 1.35700 -0.41110 cmb -0.45708 1 0 6 15 7 14 0 0 0 0
C7 6 -0.55366 -0.67813 0.71706 cmb -0.46753 1 0 12 4 7 13 0 0 0 0
C1 6 -0.84256 -0.82227 -0.78499 cmb -0.22383 1 0 3 6 5 11 0 0 0 0
C2 6 0.47600 -1.42925 -1.10866 cmb 0.50124 1 1 18 4 1 0 0 0 0 0
C6 6 -1.02738 0.67737 -1.14644 cmb -0.45246 1 0 2 10 4 9 0 0 0 0
C4 6 0.69181 0.21107 0.45807 cmb -0.17325 1 0 1 3 2 17 0 0 0 0
H3x_C3 1 2.14961 -1.38037 0.25388 cmb 0.23258 1 0 1 0 0 0 0 0 0 0
H6x_C6 1 -1.95710 0.98408 -0.66043 cmb 0.22472 1 0 6 0 0 0 0 0 0 0
H6n_C6 1 -1.09343 0.94930 -2.20301 cmb 0.22348 1 0 6 0 0 0 0 0 0 0
```


H1_C1	1	-1.70235	-1.41299	-1.11128	cmb	0.21770	1	0	4	0	0	0	0	0	0	0	0
H7s_C7	1	-0.33036	-1.63011	1.20545	cmb	0.22514	1	0	3	0	0	0	0	0	0	0	0
H7a_C7	1	-1.34588	-0.16570	1.26884	cmb	0.22667	1	0	3	0	0	0	0	0	0	0	0
H5n_C5	1	0.88691	1.73430	-1.09550	cmb	0.22436	1	0	2	0	0	0	0	0	0	0	0
H5x_C5	1	-0.25807	2.19464	0.17878	cmb	0.22333	1	0	2	0	0	0	0	0	0	0	0
H3n_C3	1	2.27695	-0.17364	-1.05946	cmb	0.23303	1	0	1	0	0	0	0	0	0	0	0
H4_C4	1	1.22737	0.59864	1.32848	cmb	0.21129	1	0	7	0	0	0	0	0	0	0	0
O_UNK_0	8	0.64131	-2.49483	-1.75450	cmb	-0.45802	1	1	5	0	0	0	0	0	0	0	0

Data file for COSMOS MD simulation (.cod) for norcamphor (1)

The cosmos data file (.cod) containing the experimental data for norcamphor prepared for the MDOC run in the program COSMOS is shown below. The file contains at the beginning lines with remarks (REMARK), which contain information about the conditions and the origin of data, the used groups and their meaning. The experimental RDCs used as constraints follow (DD_TENSORS), showing the used grouping (GROUP_MEMBERS), and fixing of the methylene protons (FIXED_DISTANCES).

Beginning of the COSMOS data file

```
$COD003
REMARK NMR parameters for Norcamphor
REMARK Norcamphor Angew Chem Int Ed Engl 2013, 52, 10309
REMARK RDC from alignment in PEOMMA/TFE-d2
REMARK Group 1: all Carbons
REMARK Group 2: all protons
REMARK Group 3: bond DD tensors - used as constraints (both atoms have to be in
group 1)
REMARK Group 4: RDC values - used as constraints (both atoms have to be in group 4)
REMARK Group 5: fixed distances
REMARK Group 6: 13C for RDC calculation
REMARK Group 7: Torsion angles for Mathematica snapshot
REMARK ordered exp. Values
RC_OPT_MOLECULE IN_MOL
RDC_OPT_MOLECULE IN_MOL
NAMES_OPT_FIT_TO EXACT
DATA_OPT_END
DD_TENSORS 10
H1_C1      C1      -0.7   -0.7    1.4     0       0       0(0.5)
H3x_C3     C3     -3.0   -3.0    6.0     0       0       0(0.7)
H3n_C3     C3     -2.5   -2.5    5.0     0       0       0(0.7)
H4_C4      C4      1.45   1.45   -2.9     0       0       0(0.3)
H5x_C5     C5      5.25   5.25  -10.5     0       0       0(0.5)
H5n_C5     C5     -2.65  -2.65   5.3     0       0       0(0.5)
H6x_C6     C6      0.95   0.95   -1.9     0       0       0(0.5)
H6n_C6     C6     -0.75  -0.75   1.5     0       0       0(0.2)
H7s_C7     C7     -2.9   -2.9    5.8     0       0       0(0.2)
H7a_C7     C7      3.55   3.55   -7.1     0       0       0(0.2)
GROUP_MEMBERS 19
^C.*$      1 all Carbons
^H.*$      2 all Protons
H[1-7].*_C[1-7] 3 DD tensor (constraints)
H[1-7].*_C[1-7] 4 RDC values
C[1-7]     4
H[3].*_C3  5 Atoms for fixed distances
H[5].*_C5  5
H[6].*_C6  5
H[7].*_C7  5
H1_C1      5
```

H4_C4	5
^C[1-7]	6 13C for RDC calc
H[34567].*_C[1-7]	7 tors angles
C[1-7]	7
H[3].*_C3	8 Atoms for fixed distances
H[5].*_C5	8
H[6].*_C6	8
H[7].*_C7	8
C[12456]	8
FIXED_DISTANCES 12	
H[3].*_C3 C4	
H[3].*_C3 C2	
H3x_C3 H3n_C3	
H[5].*_C5 C4	
H[5].*_C5 C6	
H5x_C5 H5n_C5	
H[6].*_C6 C5	
H[6].*_C6 C1	
H6x_C6 H6n_C6	
H[7].*_C7 C1	
H[7].*_C7 C4	
H7s_C7 H7a_C7	
END	

End of COSMOS data file

Data file for MSpin SVD fitting calculation for norcamphor

The data file to be used with the program MSpin to perform the singular value composition (SVD) calculation as a comparison to the outcome from the MD simulation is given below. It contains the same experimental data, but the data file format is different to the COSMOS input data file. The program MSpin allows direct probing of the prochiral assignment using the command permutations where the assignment of the methylene group protons is exchanged automatically during the SVD fit. For easy readability of the data file the atom pair labels are given as a remark, marked with # symbol.

Beginning of the MSpin data file

```
rdc_data {  
#H1 C1  
5 9 1.400 0.167  
#H3x C3  
8 11 6.000 0.233  
#H3n C3  
8 10 5.000 0.233  
#H4 C4  
2 12 -2.900 0.100  
#H5x C5  
7 13 -10.500 0.167  
#H5n C5  
7 14 5.300 0.167  
#H6x C6  
3 16 -1.900 0.167  
#H6n C6  
3 15 1.500 0.067  
#H7s C7  
6 18 5.800 0.067  
#H7a C7  
6 17 -7.100 0.067  
}
```

```
permutations {  
18 17  
}
```

End of MSpin data file

MDOC run Project file (.cos) for norcamphor

The program COSMOS requires a project file, called cosmos options file (.cos), which contains all the parameters, which define the MD simulation. The project file allows starting the MD simulations in the background and/or on a cluster environment. The project file is given below on the example of the norcamphor molecule. Some sections of the project file were removed as they are irrelevant to the molecular dynamics simulations used in this manuscript. This ensures better readability of the project file. All the deleted lines are indicated with “.....”.

Beginning of the project file

```
//-----  
// COSMOS Project File for Version: 6  
//-----  
// File Names  
//-----  
PSE_FILE cosmos.pse           // Periodic System of Elements  
FF_PARMFILE forces.par        // File with non standard force field parameters. If  
the entry is empty or forces.par: default parameters are used•  
Q_PARMFILE q631gnbo.cha       // Parameters for BPT-charge calculation  
BPT_PARMFILE HC_CC-DD.pol      // Parameters for BPT-property calculation  
LOG_FILE COSMOSLog.txt        // File for Log data output (default: COSMOSLog.txt)  
(backend)  
OUTPUT_DIR C:\COSMOS_data\NorCamp_best_withFixed_Ref_CH_Ao_HH\ // Blank|Directory for  
output files (front end)  
DATA_IMPORT_FILE              // Blank|Read NMR data and constraints from this *.cod  
or *.coo-file (backend)  
//-----  
// Bond Search Parameters  
//-----  
...  
//-----  
// Calculation of Atomic Charges  
//-----  
ChargeCalcMode 2              // Mode = 0: No Calculation | 1: EN-Charge | 2: BPT-  
Charge  
Q_CutoffRadius 30             // Cutoff radius for the charge calculation  
ChargeIncludeSet 0            // 0|n<25 Calculate charges only for this group n  
ChargeExcludeSet 0           // 0|n<25 Exclude this group n from charge calculation  
ChargedMolecule 0           // 0|1 Search for charged groups in peptides and  
proteins  
pH_Value 7                   // pH_Value for charged group search  
//-----  
// Calculation of Atomic Properties using the Bond Polarization Theory  
//-----  
BPT_CutoffRadius 30           // a>0.0: Cutoff radius for BPT property calculations  
PCalc_IncludeSet 3            // 0|n<25 calculate properties for this group
```

```

PCalc_ExcludeSet 0          // 0|n<25 exclude this group from property calculation
CS-References               // blank|Text with CS references: form E1-Mn:name
value (C-13:ppm/TMS 0.0)
BPT_PolIncludeSet 0         // 0|n<25 use only this group for bond polarization
BPT_PolExcludeSet 0         // 0|n<25 exclude this group from bond polarization
TensorCalcMode 1           // 1: Calculate full tensor | 2: Oriented sample
average | 3: Isotropic mean values
SetTensorPoints 3           // 0|n<25 calculate local order tensors for this group
PropertyKeyNumbers 1 3      // n>0 Numbers of selected data types for the property
calculation
//-----
// Parameters for the COSMOS-NMR Force Field
//-----
BondLengthOpt 1             // 0|1 Optimize bond length
BondAngleOpt 1              // 0|1 Optimize bond angles
PiBondTorsionFactor 1       // a>0 Factor to enhance the pi-torsion barrier
(default 1.0)
DiederAngleOpt 1            // 0|1 Optimize torsion angles
VanDerWaalsOpt 1            // 0|1 Optimize Van der Waals energy
TruncVDW_Repuls 0           // 0|1 Truncate the VdW repulsion to 48 times min
value (version 6)
ElectrostaticOpt 1          // 0|1 Optimize electrostatic energy
BendAngleOpt 1              // 0|1 Optimize bend angles
AllNBInteractions 1         // 0|1 include all interactions of fixed groups
NB_ElectrostaticsOnly 0     // 0|1 include only electrostatics of fixed groups
(version 6)
ELS_ForceMemoryTimeC 100    // NB_ElectrostaticsOnly?: Memory time (ps) for
electrostatic forces
FF_IncludeSet 0             // 0|n<25 run force field for this connected group
only
FF_ExcludeSet 0             // 0|n<25 exclude this connected group from force
field
FF_FixSet 0                 // 0|n<25 fix this group of atoms
FF_FixedBondsSet 5          // 0|n<25 fix all bond lengths for this group in MD
simulations
MD_FixedDistancesSet 8      // 0|n<25 fix distances as given in R-constraints for
this group in MD simulations(version 6)
FF_UnitCellSet 0            // 0|n<25 group of unit cell content
CutoffRadVDW 6              // Cutoff radius for Van der Waals interactions
CutoffRadELS 30             // Cutoff radius for electrostatic interactions
HarmonicBondPotential 1     // 0|1: Use harmonic potentials for bond forces
PeriodicBoundaryCond 0      // 0|1: Periodic box
CrystBoundaryCond 0         // 0|1: Periodic crystal lattice
BPT-PeriodicCell/Box 0      // 0|1: BPT calculation for periodic box or cell
ShiftMolToCrystCell 0      // 0|1: Shift molecules to cell in MD calculations
//-----
// Geometry Optimization using the COSMOS-NMR Force Field
//-----
MaxCycles 10000             // n: Maximum number of cycles
PictureCycles 1             // 0|n: Refresh picture after n cycles (front end)
ControlCycles 10            // 0|n: Generate log output after n cycles (front end)
ChargeCycles 1              // 0|n: Calculate BPT charges after n cycles
OptimizationMode 1          // 0: Gradient optimization | 1: conjugated gradient
optimization
StartSlope 1                // a>0 Optimization step width at start (default 1.0)

```

```

ForceEps 1e-06                // fabs(forces(cycle n)-forces(cycle n-1))<eps ?:
terminate optimization
//-----
// Snapshots in Molecular Dynamics Simulations using the COSMOS-NMR Force Field
//-----
SnapshotTypes COO DIST TORSION DD_TENS ENERGY // TYPE TYPE
...TYPE=COO|DIST|ANGLES|TORSION|RAMA|INERTIA|CHARGES|CS_ISO|CS_TENS|DD_TENS|QC_TENS|RD
C|JC|ENERGY
COO_SnapGroup 0                // 0|n<25 Group for coordinate (COO) snapshot
DIST_SnapGroupFrom 1           // 0|n<25 Distance (DIST) snapshots from this group n
of atoms
DIST_SnapGroupTo 1             // 0|n<25 Distance (DIST) snapshots to this group n of
atoms
DIST_SnapCutoff 4              // a>0.0 Cutoff radius a for distance (DIST) snapshots
ANGLES_SnapGroup 0             // 0|n<25 Angles (ANGLES) snapshots from this group n
of atoms
TORSIONS_SnapGroup 7          // 0|n<25 Torsion angles (TORSION) snapshots from this
group n of atoms
RAMA_SnapGroup 0               // 0|n<25 Ramachandran (RAMA) snapshots from this
group n of atoms
CHARGES_SnapGroup 0            // 0|n<25 Atomic charges (CHARGES) snapshots from this
group n of atoms
CS_SnapGroup 0                 // 0|n<25 Chemical shift (CS_ISO) snapshots from this
group n of atoms
BPT_TensorGroup 0 3 0          // 0|n<25 BPT tensor (CS, DD, QC) snapshots from this
group n of atoms
RDC_SnapGroup 4                // 0|n<25 RDC-Coupling snapshots from this group n of
atoms, group 0:all calculated RDC
J_SnapGroup 0                  // 0|n<25 J-Coupling snapshots from this group n of
atoms
//-----
// Property Calculation Controls in MD Simulations using the COSMOS-NMR Force Field
//-----
GroupFixedBondLength 5         // 0|n<25 Fix the bond length for this group n (set
parameter FF_FixedBondsSet for force field)
PropertyCycles 1               // 0|n: Calculate NMR properties after n cycles
EnablePropertyCalc 1           // 0|1: Enable BPT property calculation
Enable_NMR_Spec 0              // 0|1: Enable NMR spectra display (front end)
NMR_SpecCycles 10              // n Cycles for NMR spectra refresh (front end)
TimeAverageProperty 1          // 0|1: Calculate time average of BPT properties
PropertyMemoryTimeConst 200    // a>0.0 in pico sec: memory time constant for the
property average
//-----
// Temperature Controls in MD Simulations using the COSMOS-NMR Force Field
//-----
ThermostatingMode 1            // 0:No thermostating | 1:Keep temperature constant |
2: Heating or cooling
RestartMode 1                  // 0:Restart at actual temperature | 1:Start with
random velocities
StartTemperature 300           // a>0.0 Start temperature in Kelvin in the case of
RestartMode=1
TargetTemperature 300          // a>0.0 Target temperature in Kelvin (heating or
cooling)
T_CouplingTimeConst 0.02       // a>0.0 Coupling time constant to the thermostat in
pico sec

```

```

//-----
// Process Controls in MD Simulations using the COSMOS-NMR Force Field
//-----
DynaPicCycles 100          // 0|n Cycles for the picture refresh (front end)
DynaControlCycles 200      // 0|n Cycles for Log-window output or programmed stop
DataSnapshotCycles 10000   // 0|n Cycles for data snapshots
MaxTimeSteps 20000000      // n>0 Maximum number of time steps
FemtoTimeStep 0.5         // a>0.0 Verlet time step in femto sec.
DynChargeCycles 4          // 0|n Cycles for BPT atomic charge calculation
CoordSnapshotCycles 20000  // 0|n Cycles for coordinate snapshots
HeatingCoolingCycles 298   // 0<n<=MaxTimeSteps: Cycles for heating or cooling
(only if ThermostatingMode==2)
//-----
// MPI Controls in MD Simulations using the COSMOS-NMR Force Field
//-----
GlobalRemoveTransRotCyc 1000 // n Cycles for global remove of translations or
rotation (MPI backend only)
GlobalThermostatingCyc 1000 // n Cycles for global thermostating (MPI backend
only)
GlobalExchangeChargesCyc 100 // n Cycles for global BPT charge exchange (MPI
backend only)
ProcessPartitionMethod 0      // 0:Process partition of molecules |1:Sequential
partition
//-----
// Spectra and Distributions Controls in MD Simulations using the COSMOS-NMR FF
//-----
SaveNMR_Spectra 0           // n Cycles to save NMR spectra (front end)
SaveDistributionFkt 0        // n Cycles to save distribution functions (front end)
EnableCalcDistFkt 0         // 0|1: Enable the calculation of distribution
functions (front end)
EnableShowDistFkt 0         // 0|1: Enable the display of distribution functions
(front end)
EnableResetMotions 1        // 0|1: Enable the elimination of global motions
PutAllMoleculesToBox 0      // 1: All molecules are put to the periodic box |0:
Mol. with atoms outside the box are not treated periodically
//-----
// Table Output
//-----
AtNbInCoordTable 1          // 0|1: Numbering of atoms in table
SymbInCoordTable 1          // 0|1: Site name in table
PseNbInCoordTable 1         // 0|1: PSE number in table
CoordTypeInTable 0          // 0: Cartesian | 1: crystallographic coordinates
(front end)
AtNbInChargeTable 1         // 0|1: Numbering in charge table
SymbInChargeTable 1         // 0|1: Site name in charge table
PseNbInChargeTable 1        // 0|1: PSE number in charge table
CSIsoTable 1               // 0|1: Display isotropic property table
CSTensorTable 0            // 0|1: Display tensorial property table
CSAnisoTable 1             // 0|1: Display anisotropy parameters
SelectedTableType 0         // 0: All atoms | 1: Group | 2: Surrounding of atom in
property table
CentralAtInTable 1          // 0|n: Central atom n for surrounding for table type
2
GroupInTable 0              // 0|n: Group n for table type 1
RadiusInTable 1e+03         // r>0 Radius for atom surrounding for table type 2

```



```

GeoOptEnergyLog 1          // 0|1: Output of running geometry optimization to
log-window (front end) or log-file
DynamicsOutputLog 1       // 0|1: Output of running MD info to log-window (front
end) or log-file
MonteCarloOutputLog 0     // 0|1: Output of Monte-Carlo info to log-window
(front end) or log-file
TableOutputType CONSTR RCON JCON RDC // TYPE TYPE...TYPE=CHAR|BPT-PROP|JC|TENS-
O|PISEMA|ORDER|DIP|CONSTR|RDC|RCON|JCON|PSEUDO-EN|ENERGY
//-----
// Fit of Molecular Structures to Properties and NMR-Spectra
//-----
.....
//-----
// Calculation of BPT Pseudo-Forces for NMR Structure Fit
//-----
....
//-----
// Width and Weight Parameters for Distance Constraints
//-----
....
//-----
// Width and Weight Parameters for Orientational Pseudo-Forces
//-----
CS_TensorWidth 0          // a>0 Width parameter for the oriented CS constraints
fit
CS_TensorWeight 0         // a>0 Weight factor for the oriented CS pseudo forces
DD_TensorWidth 0.5        // a>0 Width parameter for the oriented DD constraints
fit
DD_TensorWeight 0.0006    // a>0 Weight factor for the oriented DD pseudo forces
Q_TensorWidth 0           // a>0 Width parameter for the oriented QC constraints
fit
Q_TensorWeight 0          // a>0 Weight factor for the oriented QC pseudo forces
//-----
// Calculation of Distribution Functions
//-----
DistanceDistrDataPoints 600 // n: Number of data points in distance distribution
graphics
CalcDistDitribution 0     // 0:1 Calculate distance distribution (front end V6)
DistanceDistrSearchRad 6   // a>0 Search radius for distance distribution
DistanceGroup 0            // 0|n<25 Group for distance distribution
DistanceGroupTo 0          // 0|n<25 Second group for distance distribution
CalcBondAnglesDist 0       // 0:1 Calculate bond angle distribution graphics
(front end V6)
BondAngleGroup 0           // 0|n<25 Group for bond angle distribution
BondAngleMin 0             // a: Minimum in bond angle graphics
BondAngleMax 180           // a: Maximum in bond angle graphics
CalcTorsionAnglesDist 0    // 0:1 Calculate torsion angle distribution graphics
(front end V6)
TorsionAngleGroup 0        // 0|n<25 Group for torsion angle distribution
TorsionAngleMin -180       // a: Minimum in torsion angle graphics
TorsionAngleMax 180        // a: Maximum in torsion angle graphics
BondAngleDistType 0        // 0: General angle distribution | 1: Bond angle
distribution
//-----
// Display of Chemical Shift Spectra

```

```

//-----
....
//-----
// Display of Quadrupolar Spectra
//-----
....
//-----
// Display of Dipolar Spectra
//-----
.....
//-----
// Width and Weight Factors of the RDC Distance Fit
//-----
.....
//-----
// Width and Weight Factors of the Orientational RDC Fit
//-----
.....
//-----
// RDC Calculation
//-----
.....
//-----
// Oriented Sample
//-----
OrientedTensCalcMode 1          // 0:None |1: Full tensor |2: Mean value for fast
rotation around director |3: Full tensor + rot. distribution
DirectorTiltAngle 0            // 0<= a <=180 Director tilt angle
SampleOrderParameter 0.001     // 0<= a <=1.0 Order parameter of oriented sample
//-----
// Global Width Settings
//-----
UseErrorsAsWidth 1             // 0|1 Use the experimental errors as width for DD,
RDC, R and J constraints in MD simulations
//-----
// Import and Export Options
//-----
.....
//-----
// Parameters for 3J Couplings
//-----
.....

```

End project file

Command to start the MD simulation using the COSMOS backend

The command line for starting the MDOC run in the background and/or in a cluster environment is given below on the example of norcamphor. It indicates the location of all the necessary files: program executable, project file (.cos), data file (.cod), configuration directory, data directory to store the output files and the cosmos coordinate file (.coo).

Beginning of the script

```
/home/kit/USER/COSMOS/bin/cosback.x86_64-STATIC -dw -c  
/home/kit/USER/Norcamphor/NorCamp_best_withFixed_Ref_CH_Ao_HH_0.00045DD_width.cos  
-a  
/home/kit/USER/Norcamphor/norcamphor_withFixed_Ao_HH_cor.cod -f  
/home/kit/USER/COSMOS/config -y  
/work/kit/USER/NorCamp_best_withFixed_Ref_CH_Ao_HH_0.00045DD_width_corr_best_Ref_  
CH_Ao  
/home/kit/USER/Norcamphor/norcamphor_raw_opt_best_Ref_CH_Ao.coo
```

End of the script

Synthetic spiroindene derivative

Experimental data ($^1D_{CH}$) for synthetic spiroindene derivative 2

Table S2. Experimental one bond $^1D_{CH}$ in Hz for synthetic spiroindene derivative in PDMS/ $CDCl_3$ as given in [2], where the experimental errors in Hz are obtained directly from the authors.

	$\delta_{1H}/[ppm]^*$	$\delta_{13C}/[ppm]$	$^1T_{CH}/[Hz]$	$^1D_{CH}/[Hz]$	Error [Hz]
C3-H3				-0.30	1.0
C4-H4				4.90	1.0
C5-H5				-2.05	2.0
C2-H2				-2.20	2.0
C1a-H1a				-2.00	2.0
C6-Ha6				-1.90	1.0
C6-Hb6				-3.50	1.0
C6a-H6a				-0.20	2.0
C4'-H4'				-1.70	1.0
C5'-H5'				6.40	1.0
C6'-H6'				-1.25	1.5
C7'-H7'				-1.10	1.0

*- the chemical shift data as well as the total one-bond coupling is not available from the used literature sources.

Coordinates files of the spiroindene

As in the case of the spiroindene molecule **2**, only two possible relative configurations are possible.

Corresponding pdb-files for the right and the wrong configuration are given below:

Coordinates of spiroindene in pdb-file format (wrong configuration)

```
HEADER      NO HEADER DEFINED AND DEFAULT DATE USED          01-JAN-00
AUTHOR      PDB FILE FORMAT GENERATED BY COSMOS
CRYST1      1.000    1.000    1.000    90.000    90.000    90.000 P1
COMPND
REMARK      CREATED FILE CONTAINS ONLY BASIC MOLECULAR DATA
REMARK CELL  1.0000  1.0000  1.0000  90.000  90.000  90.000  0.0000  0.0000
0.0000
REMARK SPGROUP P1
HETATM      1  C2P NOP A  1      0.808  2.039  1.225  1.00  0.00      C
HETATM      2  C6P NOP A  1      0.943 -2.652  2.569  1.00  0.00      C
HETATM      3  C5P NOP A  1      2.329 -2.352  2.653  1.00  0.00      C
HETATM      4  C3  NOP A  1     -3.562 -2.208 -0.666  1.00  0.00      C
HETATM      5  C4  NOP A  1     -4.247 -2.448  0.556  1.00  0.00      C
HETATM      6  C4P NOP A  1      2.797 -1.048  2.349  1.00  0.00      C
HETATM      7  C3P NOP A  1      2.183  1.401  1.587  1.00  0.00      C
HETATM      8  C6  NOP A  1     -2.650  0.420  2.674  1.00  0.00      C
HETATM      9  C5  NOP A  1     -4.013 -1.624  1.688  1.00  0.00      C
HETATM     10  C2  NOP A  1     -2.633 -1.140 -0.775  1.00  0.00      C
HETATM     11  C5a NOP A  1     -3.089 -0.560  1.571  1.00  0.00      C
HETATM     12  C1b NOP A  1     -2.406 -0.323  0.358  1.00  0.00      C
HETATM     13  C6a NOP A  1     -1.661  1.370  1.963  1.00  0.00      C
HETATM     14  C1a NOP A  1     -1.459  0.880  0.443  1.00  0.00      C
HETATM     15  C7P NOP A  1      0.007 -1.656  2.184  1.00  0.00      C
HETATM     16  C3a NOP A  1      1.857 -0.061  1.968  1.00  0.00      C
HETATM     17  C1P NOP A  1     -0.243  0.927  1.443  1.00  0.00      C
HETATM     18  C7a NOP A  1      0.474 -0.352  1.890  1.00  0.00      C
HETATM     19  H1a C1a A  1     -1.606  1.712 -0.250  1.00  0.00      H
HETATM     20  H2  C2  A  1     -2.103 -0.950 -1.712  1.00  0.00      H
HETATM     21  HA2PC2P A  1      0.803  2.371  0.184  1.00  0.00      H
HETATM     22  HB2PC2P A  1      0.602  2.895  1.873  1.00  0.00      H
HETATM     23  H3  C3  A  1     -3.750 -2.852 -1.529  1.00  0.00      H
HETATM     24  HB3PC3P A  1      2.866  1.419  0.734  1.00  0.00      H
HETATM     25  HA3PC3P A  1      2.646  1.910  2.437  1.00  0.00      H
HETATM     26  H4  C4  A  1     -4.956 -3.277  0.626  1.00  0.00      H
HETATM     27  H4P C4P A  1      3.862 -0.807  2.404  1.00  0.00      H
HETATM     28  H5  C5  A  1     -4.528 -1.810  2.635  1.00  0.00      H
HETATM     29  H5P C5P A  1      3.038 -3.129  2.949  1.00  0.00      H
HETATM     30  HB6 C6  A  1     -3.515  0.972  3.051  1.00  0.00      H
HETATM     31  HA6 C6  A  1     -2.159 -0.105  3.498  1.00  0.00      H
HETATM     32  H6P C6P A  1      0.594 -3.661  2.801  1.00  0.00      H
HETATM     33  H6a C6a A  1     -1.849  2.445  2.025  1.00  0.00      H
HETATM     34  H7P C7P A  1     -1.053 -1.916  2.122  1.00  0.00      H
CONECT      1    22    17    7    21
CONECT      2    15    3    32
```


HETATM	11	C3a	NOP	A	1	2.184	-0.893	-0.024	1.00	0.00	C
HETATM	12	C5a	NOP	A	1	-2.675	0.789	1.784	1.00	0.00	C
HETATM	13	C1b	NOP	A	1	-2.532	-0.345	0.954	1.00	0.00	C
HETATM	14	C6a	NOP	A	1	-0.904	1.336	0.198	1.00	0.00	C
HETATM	15	C1a	NOP	A	1	-1.435	-0.153	-0.099	1.00	0.00	C
HETATM	16	C7a	NOP	A	1	1.146	-0.190	-0.676	1.00	0.00	C
HETATM	17	C2P	NOP	A	1	0.508	-0.425	1.731	1.00	0.00	C
HETATM	18	C1P	NOP	A	1	0.052	0.096	0.352	1.00	0.00	C
HETATM	19	H1a	C1a	A	1	-1.668	-0.287	-1.159	1.00	0.00	H
HETATM	20	H2	C2	A	1	-3.210	-2.372	0.509	1.00	0.00	H
HETATM	21	HB2PC2P	A	1	0.633	0.408	2.428	1.00	0.00	H	
HETATM	22	HA2PC2P	A	1	-0.214	-1.134	2.144	1.00	0.00	H	
HETATM	23	H3	C3	A	1	-4.918	-2.364	2.366	1.00	0.00	H
HETATM	24	HA3PC3P	A	1	1.816	-2.201	1.671	1.00	0.00	H	
HETATM	25	HB3PC3P	A	1	2.671	-0.690	2.087	1.00	0.00	H	
HETATM	26	H4	C4	A	1	-5.177	-0.350	3.835	1.00	0.00	H
HETATM	27	H4P	C4P	A	1	4.137	-1.848	-0.234	1.00	0.00	H
HETATM	28	H5	C5	A	1	-3.731	1.686	3.471	1.00	0.00	H
HETATM	29	H5P	C5P	A	1	4.303	-1.297	-2.691	1.00	0.00	H
HETATM	30	HB6	C6	A	1	-2.249	2.805	1.099	1.00	0.00	H
HETATM	31	HA6	C6	A	1	-1.026	2.152	2.228	1.00	0.00	H
HETATM	32	H6P	C6P	A	1	2.462	-0.043	-3.835	1.00	0.00	H
HETATM	33	H6a	C6a	A	1	-0.801	1.939	-0.708	1.00	0.00	H
HETATM	34	H7P	C7P	A	1	0.417	0.677	-2.550	1.00	0.00	H
CONNECT	1	5	2	29							
CONNECT	2	9	1	32							
CONNECT	3	10	4	23							
CONNECT	4	8	3	26							
CONNECT	5	11	1	27							
CONNECT	6	25	17	11	24						
CONNECT	7	31	14	12	30						
CONNECT	8	12	4	28							
CONNECT	9	16	2	34							
CONNECT	10	13	3	20							
CONNECT	11	5	6	16							
CONNECT	12	7	8	13							
CONNECT	13	10	12	15							
CONNECT	14	18	7	15	33						
CONNECT	15	18	13	14	19						
CONNECT	16	9	11	18							
CONNECT	17	22	18	6	21						
CONNECT	18	14	15	16	17						
CONNECT	19	15									
CONNECT	20	10									
CONNECT	21	17									
CONNECT	22	17									
CONNECT	23	3									
CONNECT	24	6									
CONNECT	25	6									
CONNECT	26	4									
CONNECT	27	5									
CONNECT	28	8									
CONNECT	29	1									
CONNECT	30	7									
CONNECT	31	7									

CONNECT	32	2							
CONNECT	33	14							
CONNECT	34	9							
MASTER		0	0	0	0	0	0	0	0
END									

Coordinates of spiroindene in coo-file format (wrong configuration)

The coordinates of spiroindene in a coo-file format generated as an input for the program COSMOS with the wrong configuration is given below.

```
$COO006
CELL  1.0000  1.0000  1.0000  90.000  90.000  90.000  0.0000  0.0000  0.0000
NAME
SPGROUP P1
GROUP_TEXT 1 all Carbons
GROUP_TEXT 2 all Protons
GROUP_TEXT 3 DDs
GROUP_TEXT 5 Fix CH-bond
GROUP_TEXT 6 13C for RDC calculation
GROUP_TEXT 7 Torsion angles
GROUP_TEXT 8 Fix distances
ATOMS 34
C7aP 6  0.47428 -0.35190  1.88971 smb 193 1 3 4 3 2 0 0 0 0 0
C1P 6 -0.24254  0.92720  1.44303 smb 193 1 0 18 6 5 1 0 0 0 0
C3aP 6  1.85651 -0.06094  1.96756 smb 193 1 5 13 12 1 0 0 0 0 0
C7P 6  0.00684 -1.65568  2.18437 smb 33 1 3 1 17 34 0 0 0 0 0
C1a 6 -1.45907  0.88012  0.44308 smb 225 1 0 2 7 6 19 0 0 0 0
C6a 6 -1.66130  1.37046  1.96251 smb 225 1 0 2 11 5 20 0 0 0 0
C1b 6 -2.40570 -0.32260  0.35764 smb 65 1 3 9 8 5 0 0 0 0 0
C5a 6 -3.08894 -0.56024  1.57067 smb 193 1 6 11 10 7 0 0 0 0 0
C2 6 -2.63303 -1.13989 -0.77499 smb 33 1 3 7 15 33 0 0 0 0 0
C5 6 -4.01311 -1.62437  1.68839 smb 33 1 3 8 14 32 0 0 0 0 0
C6 6 -2.65005  0.42000  2.67438 smb 97 1 0 6 22 8 21 0 0 0 0
C3P 6  2.18327  1.40132  1.58723 smb 193 1 0 3 31 18 30 0 0 0 0
C4P 6  2.79706 -1.04795  2.34913 smb 33 1 3 3 16 29 0 0 0 0 0
C4 6 -4.24716 -2.44819  0.55557 smb 33 1 3 10 15 28 0 0 0 0 0
C3 6 -3.56164 -2.20805 -0.66556 smb 33 1 3 9 14 27 0 0 0 0 0
```

C5P 6 2.32890 -2.35189 2.65293 smb 33 1 3 13 17 26 0 0 0 0 0
 C6P 6 0.94284 -2.65156 2.56871 smb 33 1 3 4 16 25 0 0 0 0 0
 C2P 6 0.80812 2.03927 1.22504 smb 193 1 0 23 2 12 24 0 0 0 0
 H1a_C1a 1 -1.60574 1.71206 -0.25047 smb 22 1 0 5 0 0 0 0 0 0 0
 H6a_C6a 1 -1.84860 2.44546 2.02536 smb 22 1 0 6 0 0 0 0 0 0 0
 Ha6_C6 1 -2.15924 -0.10519 3.49774 smb 150 1 0 11 0 0 0 0 0 0 0
 Hb6_C6 1 -3.51498 0.97191 3.05114 smb 150 1 0 11 0 0 0 0 0 0 0
 Hb2P_C2P 1 0.60180 2.89529 1.87259 smb 146 1 0 18 0 0 0 0 0 0 0
 Ha2P_C2P 1 0.80350 2.37114 0.18366 smb 146 1 0 18 0 0 0 0 0 0 0
 H6P_C6P 1 0.59384 -3.66099 2.80090 smb 22 1 0 17 0 0 0 0 0 0 0
 H5P_C5P 1 3.03797 -3.12926 2.94884 smb 22 1 0 16 0 0 0 0 0 0 0
 H3_C3 1 -3.74978 -2.85156 -1.52878 smb 22 1 0 15 0 0 0 0 0 0 0
 H4_C4 1 -4.95575 -3.27738 0.62618 smb 22 1 0 14 0 0 0 0 0 0 0
 H4P_C4P 1 3.86182 -0.80722 2.40357 smb 22 1 0 13 0 0 0 0 0 0 0
 Ha3P_C3P 1 2.64624 1.90982 2.43679 smb 146 1 0 12 0 0 0 0 0 0 0
 Hb3P_C3P 1 2.86581 1.41915 0.73372 smb 146 1 0 12 0 0 0 0 0 0 0
 H5_C5 1 -4.52765 -1.80990 2.63469 smb 22 1 0 10 0 0 0 0 0 0 0
 H2_C2 1 -2.10349 -0.94969 -1.71204 smb 22 1 0 9 0 0 0 0 0 0 0
 H7P_C7P 1 -1.05276 -1.91634 2.12154 smb 22 1 0 4 0 0 0 0 0 0 0

SITE_NAMES

1 C7aP	18 C2P	19 H1a_C1a	20
H6a_C6a	21 Ha6_C6		
22 Hb6_C6	23 Hb2P_C2P	24 Ha2P_C2P	25
H6P_C6P	26 H5P_C5P		
27 H3_C3	28 H4_C4	29 H4P_C4P	30
Ha3P_C3P	31 Hb3P_C3P		
32 H5_C5	33 H2_C2	34 H7P_C7P	

DD_TENSORS 12

19 5	1.00000	1.00000	-2.00000	0.00000	0.00000	0.00000(2)
20 6	0.10000	0.10000	-0.20000	0.00000	0.00000	0.00000(2)
21 11	0.95000	0.95000	-1.90000	0.00000	0.00000	0.00000(1)
22 11	1.75000	1.75000	-3.50000	0.00000	0.00000	0.00000(1)
25 17	0.62500	0.62500	-1.25000	0.00000	0.00000	0.00000(1.5)
26 16	-3.20000	-3.20000	6.40000	0.00000	0.00000	0.00000(1)
27 15	0.15000	0.15000	-0.30000	0.00000	0.00000	0.00000(1)

28	14	-2.45000	-2.45000	4.90000	0.00000	0.00000	0.00000 (1)
29	13	0.85000	0.85000	-1.70000	0.00000	0.00000	0.00000 (1)
32	10	1.02500	1.02500	-2.05000	0.00000	0.00000	0.00000 (2)
33	9	1.10000	1.10000	-2.20000	0.00000	0.00000	0.00000 (2)
34	4	0.55000	0.55000	-1.10000	0.00000	0.00000	0.00000 (1)

FIXED_DISTANCES 8

1 5 2.7108 6 2.74454

18 5 2.66369 6 2.66256

21 6 2.18687 8 2.18747 22 1.78819

22 6 2.18634 8 2.17274

23 2 2.18422 12 2.19418

24 2 2.18293 12 2.19416 23 1.77986

30 3 2.17434 18 2.2054 31 1.78589

31 3 2.17525 18 2.20455

Coordinates of spiroindene in coo-file format (correct configuration)

The coordinates of spiroindene in a coo-file format generated as an input for the program COSMOS with the correct configuration is given below.

```
$COO006
CELL  1.0000  1.0000  1.0000  90.000  90.000  90.000  0.0000  0.0000  0.0000
NAME
GROUP_TEXT 1 all Carbons
GROUP_TEXT 2 all Protons
GROUP_TEXT 3 DDs
GROUP_TEXT 5 Fix CH-bond
GROUP_TEXT 6 13C for RDC calculation
GROUP_TEXT 7 Torsion angles
GROUP_TEXT 8 Fix distances
ATOMS 34
C1P 6  0.05227  0.09614  0.35201 smb 193 1 0 5 4 3 2 0 0 0 0
C2P 6  0.50790 -0.42486  1.73105 smb 193 1 0 33 1 13 34 0 0 0 0
C7aP 6  1.14646 -0.18958 -0.67615 smb 193 1 3 10 8 1 0 0 0 0 0
C1a 6 -1.43540 -0.15284 -0.09901 smb 225 1 0 1 6 5 19 0 0 0 0
C6a 6 -0.90374  1.33585  0.19807 smb 225 1 0 1 12 4 20 0 0 0 0
C1b 6 -2.53245 -0.34516  0.95407 smb 65 1 3 9 7 4 0 0 0 0 0
C5a 6 -2.67471  0.78906  1.78434 smb 193 1 6 12 11 6 0 0 0 0 0
C3aP 6  2.18421 -0.89316 -0.02447 smb 193 1 5 14 13 3 0 0 0 0 0
C2 6 -3.33167 -1.49570  1.14964 smb 33 1 3 6 16 32 0 0 0 0 0
C7P 6  1.22297  0.13178 -2.05170 smb 33 1 3 3 17 31 0 0 0 0 0
C5 6 -3.62620  0.80578  2.83112 smb 33 1 3 7 15 30 0 0 0 0 0
C6 6 -1.69388  1.91193  1.39641 smb 97 1 0 21 5 7 22 0 0 0 0
C3P 6  1.87933 -1.12796  1.47367 smb 193 1 0 28 2 8 29 0 0 0 0
C4P 6  3.33544 -1.30143 -0.73873 smb 33 1 3 8 18 27 0 0 0 0 0
C4 6 -4.43617 -0.34370  3.03139 smb 33 1 3 11 16 26 0 0 0 0 0
C3 6 -4.28965 -1.48569  2.19774 smb 33 1 3 9 15 25 0 0 0 0 0
```

C6P 6 2.37685 -0.27708 -2.77101 smb 33 1 3 10 18 24 0 0 0 0 0
 C5P 6 3.42305 -0.98792 -2.12156 smb 33 1 3 14 17 23 0 0 0 0 0
 H1a_C1a 1 -1.66773 -0.28723 -1.15854 smb 22 1 0 4 0 0 0 0 0 0 0
 H6a_C6a 1 -0.80132 1.93924 -0.70751 smb 22 1 0 5 0 0 0 0 0 0 0
 Ha6_C6 1 -1.02622 2.15198 2.22783 smb 150 1 0 12 0 0 0 0 0 0 0
 Hb6_C6 1 -2.24898 2.80522 1.09883 smb 150 1 0 12 0 0 0 0 0 0 0
 H5P_C5P 1 4.30338 -1.29726 -2.69074 smb 22 1 0 18 0 0 0 0 0 0 0
 H6P_C6P 1 2.46162 -0.04342 -3.83537 smb 22 1 0 17 0 0 0 0 0 0 0
 H3_C3 1 -4.91758 -2.36425 2.36647 smb 22 1 0 16 0 0 0 0 0 0 0
 H4_C4 1 -5.17659 -0.35041 3.83537 smb 22 1 0 15 0 0 0 0 0 0 0
 H4P_C4P 1 4.13678 -1.84753 -0.23447 smb 22 1 0 14 0 0 0 0 0 0 0
 Hb3P_C3P 1 2.67087 -0.69039 2.08738 smb 146 1 0 13 0 0 0 0 0 0 0
 Ha3P_C3P 1 1.81579 -2.20114 1.67087 smb 146 1 0 13 0 0 0 0 0 0 0
 H5_C5 1 -3.73121 1.68587 3.47071 smb 22 1 0 11 0 0 0 0 0 0 0
 H7P_C7P 1 0.41703 0.67663 -2.54994 smb 22 1 0 10 0 0 0 0 0 0 0
 H2_C2 1 -3.20959 -2.37248 0.50855 smb 22 1 0 9 0 0 0 0 0 0 0
 Ha2P_C2P 1 -0.21396 -1.13404 2.14412 smb 146 1 0 2 0 0 0 0 0 0 0
 Hb2P_C2P 1 0.63346 0.40798 2.42765 smb 146 1 0 2 0 0 0 0 0 0 0

SITE_NAMES

2 C2P	3 C7aP	19 H1a_C1a	20
H6a_C6a	21 Ha6_C6		
22 Hb6_C6	23 H5P_C5P	24 H6P_C6P	25
H3_C3	26 H4_C4		
27 H4P_C4P	28 Hb3P_C3P	29 Ha3P_C3P	30
H5_C5	31 H7P_C7P		
32 H2_C2	33 Ha2P_C2P	34 Hb2P_C2P	

DD_TENSORS 12

19 4	1.00000	1.00000	-2.00000	0.00000	0.00000	0.00000(2)
20 5	0.10000	0.10000	-0.20000	0.00000	0.00000	0.00000(2)
21 12	0.95000	0.95000	-1.90000	0.00000	0.00000	0.00000(1)
22 12	1.75000	1.75000	-3.50000	0.00000	0.00000	0.00000(1)
23 18	-3.20000	-3.20000	6.40000	0.00000	0.00000	0.00000(1)
24 17	0.62500	0.62500	-1.25000	0.00000	0.00000	0.00000(1.5)
25 16	0.15000	0.15000	-0.30000	0.00000	0.00000	0.00000(1)
26 15	-2.45000	-2.45000	4.90000	0.00000	0.00000	0.00000(1)

27	14	0.85000	0.85000	-1.70000	0.00000	0.00000	0.00000 (1)
30	11	1.02500	1.02500	-2.05000	0.00000	0.00000	0.00000 (2)
31	10	0.55000	0.55000	-1.10000	0.00000	0.00000	0.00000 (1)
32	9	1.10000	1.10000	-2.20000	0.00000	0.00000	0.00000 (2)

FIXED_DISTANCES 8

2 4 2.68319 5 2.72816

3 4 2.64583 5 2.70084

21 5 2.19112 7 2.18443 22 1.78788

22 5 2.18634 7 2.17165

28 2 2.20815 8 2.17666

29 2 2.20666 8 2.17272 28 1.78522

33 1 2.18995 13 2.19805 34 1.78223

34 1 2.17791 13 2.19576

Data file for COSMOS MD simulation (.cod) for spiroindene (2)

The cosmos data file (.cod) containing the experimental data for spiroindene prepared for the MDOC run in the program COSMOS is shown below. The file contains at the beginning lines with remarks (REMARK), which contains information about the conditions and the origin of data, the used groups and their meaning. The experimental RDCs used as constraints follow (DD_TENSORS), showing the used grouping (GROUP_MEMBERS), and fixing of the methylene protons (FIXED_DISTANCES). In this case an extra fixing is required to maintain the hybridisation of the carbon at the spiro position.

Beginning of the COSMOS data file

```
$COD003
REMARK Dipolar Couplings for Spiroindene taken from J.Am.Chem.Soc. 126 (2004),
45, 14690-14691.
REMARK "Stretched Polydimethylsiloxane Gels as NMR-Alignment Media for Apolar and
Weakly Polar Organic Solvents: Ideal tool for Measuring RDCs at Low Molecular
Concentrations"
REMARK Errors taken from PALES Data File
REMARK DDs added
REMARK Group 1,2,3,5,6,7,8 added
REMARK added Spirocarbons C2P, C7aP, C[16]a for avoiding flipping into group 8
(former methylene fixing)
REMARK V1.1
RC_OPT_MOLECULE IN_MOL
RDC_OPT_MOLECULE IN_MOL
NAMES_OPT_FIT_TO EXACT
DATA_OPT_END
DD_TENSORS 12
H3_C3 C3      0.15   0.15  -0.30   0 0 0(1.0)
H4_C4 C4     -2.45  -2.45   4.90   0 0 0(1.0)
H5_C5 C5      1.025  1.025  -2.05   0 0 0(2.0)
H2_C2 C2      1.10   1.10  -2.20   0 0 0(2.0)
H1a_C1a C1a   1.00   1.00  -2.00   0 0 0(2.0)
Ha6_C6 C6      0.95   0.95  -1.90   0 0 0(1.0)
Hb6_C6 C6      1.75   1.75  -3.50   0 0 0(1.0)
H6a_C6a C6a    0.10   0.10  -0.20   0 0 0(2.0)
H4P_C4P C4P    0.85   0.85  -1.70   0 0 0(1.0)
H5P_C5P C5P   -3.20  -3.20   6.40   0 0 0(1.0)
H6P_C6P C6P    0.625  0.625  -1.25   0 0 0(1.5)
H7P_C7P C7P    0.55   0.55  -1.10   0 0 0(1.0)
FIXED_DISTANCES 9
H[ab]2P_C2P    C[13]P
Ha2P_C2P       Hb2P_C2P
H[ab]3P_C3P    C3aP
H[ab]3P_C3P    C2P
Ha3P_C3P       Hb3P_C3P
H[ab]6_C6      C[56]a
```

```

Ha6_C6          Hb6_C6
C7aP            C[16]a
C2P             C[16]a
GROUP_MEMBERS 22
C.*$            1 all Carbons
H.*$            2 all Protons
H[2-5]_C[2-5]   3 DDs
H[ab]6_C6       3
H[16]a_C[16]a   3
H[4-7]P_C[4-7]P 3
H.*$            5 Fix CH-bond
C[16]a          6 13C for RDC calculation
C[2-6]          6
C[4-7]P         6
Cl[abP]         7 Torsion angles
C[23]P          7
C[37]aP         7
C[56]a          7
C6              7
H[ab][23]P_C[23]P 8 Fix distances
C[123]P         8
C3aP            8
H[ab]6_C6       8
C[56]a          8
C7aP            8
C[16]a          8
END

```

End of COSMOS data file

Staurosporine

Experimental data for staurosporine

Table S3. Experimental data for staurosporine in dPS/CDCl₃ as obtained from [3]

	$\delta_{1H}/[\text{ppm}]$	$\delta_{13C}/[\text{ppm}]$	$^1T_{CH}/[\text{Hz}]$	$^1D_{CH}/[\text{Hz}]$	Error [Hz]
C3'-H3'	3.87	84.0	120.5	-19.8	5.0
C4'-H4'	3.33	50.5	131.5	-3.7	1.0
C5'-H5'a	2.70	30.1	139.2	7.5	3.2
C6'-H6'	6.52	80.2	165.1	5.8	1.1
C2'-HMe	2.37	30.0	126.0	-3.2	1.0
C1-H1	7.23	107.0	130.8	-27.2	2.5
C2-H2	7.43	125.2	147.0	-11.1	7.6
C3-H3	7.32	119.9	162.3	1.7	4.2
C4-H4	9.40	126.7	137.9	-27.1	1.0
C8-H8	7.83	120.8	132.8	-25.3	1.0
C9-H9	7.28	120.1	148.0	-12.9	5.4
C10-H10	7.38	124.3	162.2	2.6	3.6
C11-H11	7.88	115.2	137.1	-25.4	1.1

Coordinates of staurosporine (3) in pdb file format

The coordinates of the staurosporine **3** in a pdb-file format generated as an output from the program COSMOS with the correct configuration and a starting chair conformation is given below. This configuration is marked as *Ref* throughout the manuscript.

```
HEADER      NO HEADER DEFINED AND DEFAULT DATE USED          01-JAN-00
AUTHOR      PDB FILE FORMAT GENERATED BY COSMOS
CRYST1      1.000      1.000      1.000      90.000      90.000      90.000  4
COMPND
REMARK      CREATED FILE CONTAINS ONLY BASIC MOLECULAR DATA
REMARK CELL  1.0000  1.0000  1.0000  90.000  90.000  90.000  0.0000 -0.7736
0.3485
REMARK SPGROUP 4
REMARK OPERATION CFF geometry optimization
REMARK ENERGY 1746.24
REMARK FORCE_FIELD_ENERGIES BondEn=20.0897 AngleEn=524.996 TorsionEn=968.372
PiTorsionEn=2.24663 CoulombEn=154.058 VdWEn=76.4751
HETATM      1  O3p  NOP  A      1      7.313      3.655      0.511      1.00      0.00      O
HETATM      2  O5   NOP  A      1     11.712      5.937      8.474      1.00      0.00      O
HETATM      3  O1   NOP  A      1      9.895      6.354      1.022      1.00      0.00      O
HETATM      4  N4   NOP  A      1      9.577      2.924      2.528      1.00      0.00      N
HETATM      5  N13  NOP  A      1     11.343      5.716      2.952      1.00      0.00      N
HETATM      6  N12  NOP  A      1      8.086      5.887      2.705      1.00      0.00      N
HETATM      7  N6   NOP  A      1      9.398      6.034      8.610      1.00      0.00      N
HETATM      8  C   CH3  A      1      7.691      6.701      0.348      1.00      0.00      C
HETATM      9  CNM  NOP  A      1     10.555      1.995      3.146      1.00      0.00      C
HETATM     10  COM  NOP  A      1      6.788      2.914      1.634      1.00      0.00      C
HETATM     11  C6p  NOP  A      1     11.080      5.646      1.483      1.00      0.00      C
HETATM     12  C5p  NOP  A      1     11.078      4.219      0.886      1.00      0.00      C
HETATM     13  C4p  NOP  A      1      9.760      3.438      1.132      1.00      0.00      C
HETATM     14  C3p  NOP  A      1      8.597      4.338      0.611      1.00      0.00      C
HETATM     15  C2p  NOP  A      1      8.561      5.773      1.241      1.00      0.00      C
HETATM     16  C13  NOP  A      1     12.592      5.581      3.547      1.00      0.00      C
HETATM     17  C12  NOP  A      1     10.392      5.805      3.957      1.00      0.00      C
HETATM     18  C12  NOP  A      1      8.930      5.882      3.827      1.00      0.00      C
HETATM     19  C11  NOP  A      1      6.770      5.903      3.207      1.00      0.00      C
HETATM     20  C11  NOP  A      1      5.452      5.873      2.602      1.00      0.00      C
HETATM     21  C10  NOP  A      1      4.273      5.913      3.395      1.00      0.00      C
HETATM     22  C9   NOP  A      1      4.328      5.947      4.806      1.00      0.00      C
HETATM     23  C8   NOP  A      1      5.576      5.956      5.461      1.00      0.00      C
HETATM     24  C7c  NOP  A      1      6.776      5.939      4.665      1.00      0.00      C
HETATM     25  C7b  NOP  A      1      8.166      5.935      5.072      1.00      0.00      C
HETATM     26  C7a  NOP  A      1      8.800      5.957      6.372      1.00      0.00      C
HETATM     27  C7   NOP  A      1      8.196      6.022      7.754      1.00      0.00      C
HETATM     28  C5   NOP  A      1     10.552      5.953      7.923      1.00      0.00      C
HETATM     29  C4c  NOP  A      1     10.235      5.893      6.497      1.00      0.00      C
HETATM     30  C4b  NOP  A      1     11.043      5.785      5.271      1.00      0.00      C
HETATM     31  CA4  NOP  A      1     12.467      5.634      4.995      1.00      0.00      C
HETATM     32  C4   NOP  A      1     13.639      5.534      5.826      1.00      0.00      C
HETATM     33  C3   NOP  A      1     14.904      5.376      5.214      1.00      0.00      C
```

HETATM	34	C2	NOP	A	1	15.034	5.314	3.806	1.00	0.00	C
HETATM	35	C1	NOP	A	1	13.898	5.411	2.958	1.00	0.00	C
HETATM	36	H	N4	A	1	9.458	3.707	3.177	1.00	0.00	H
HETATM	37	HMe	NOP	A	1	6.667	6.342	0.199	1.00	0.00	H
HETATM	38	HMe	NOP	A	1	7.646	7.720	0.761	1.00	0.00	H
HETATM	39	HMe	NOP	A	1	8.119	6.786	-0.663	1.00	0.00	H
HETATM	40	H6p	NOP	A	1	11.922	6.183	1.019	1.00	0.00	H
HETATM	41	H5p	NOP	A	1	11.959	3.647	1.217	1.00	0.00	H
HETATM	42	H5p	NOP	A	1	11.197	4.327	-0.204	1.00	0.00	H
HETATM	43	H4p	NOP	A	1	9.794	2.540	0.493	1.00	0.00	H
HETATM	44	H3p	NOP	A	1	8.844	4.512	-0.449	1.00	0.00	H
HETATM	45	H11	NOP	A	1	5.300	5.804	1.539	1.00	0.00	H
HETATM	46	H10	NOP	A	1	3.308	5.911	2.908	1.00	0.00	H
HETATM	47	H9	NOP	A	1	3.414	5.964	5.384	1.00	0.00	H
HETATM	48	H8	NOP	A	1	5.614	5.972	6.540	1.00	0.00	H
HETATM	49	H7a	NOP	A	1	7.575	5.138	7.963	1.00	0.00	H
HETATM	50	H7b	NOP	A	1	7.597	6.935	7.896	1.00	0.00	H
HETATM	51	H6	NOP	A	1	9.352	6.090	9.640	1.00	0.00	H
HETATM	52	H4	NOP	A	1	13.570	5.575	6.902	1.00	0.00	H
HETATM	53	H3	NOP	A	1	15.787	5.301	5.833	1.00	0.00	H
HETATM	54	H2	NOP	A	1	16.014	5.190	3.368	1.00	0.00	H
HETATM	55	H1	NOP	A	1	14.027	5.359	1.886	1.00	0.00	H
HETATM	56	HNH	NOP	A	1	10.687	1.093	2.530	1.00	0.00	H
HETATM	57	HNH	NOP	A	1	10.199	1.677	4.137	1.00	0.00	H
HETATM	58	HOM	NOP	A	1	7.357	1.988	1.803	1.00	0.00	H
HETATM	59	HOM	NOP	A	1	5.754	2.614	1.411	1.00	0.00	H
HETATM	60	HOM	NOP	A	1	6.773	3.481	2.572	1.00	0.00	H
HETATM	61	HNH	NOP	A	1	11.539	2.469	3.284	1.00	0.00	H
CONECT	1	10	14								
CONECT	2	28									
CONECT	3	11	15								
CONECT	4	36	9	13							
CONECT	5	11	16	17							
CONECT	6	15	18	19							
CONECT	7	51	27	28							
CONECT	8	37	38	39	15						
CONECT	9	61	56	4	57						
CONECT	10	59	58	60	1						
CONECT	11	40	12	5	3						
CONECT	12	41	42	11	13						
CONECT	13	43	12	14	4						
CONECT	14	44	13	15	1						
CONECT	15	8	14	6	3						
CONECT	16	31	35	5							
CONECT	17	18	30	5							
CONECT	18	17	25	6							
CONECT	19	20	24	6							
CONECT	20	45	19	21							
CONECT	21	46	20	22							
CONECT	22	47	21	23							
CONECT	23	48	22	24							
CONECT	24	19	23	25							
CONECT	25	18	24	26							
CONECT	26	25	27	29							
CONECT	27	49	50	26	7						

CONECT	28	29	7	2					
CONECT	29	26	28	30					
CONECT	30	17	29	31					
CONECT	31	16	30	32					
CONECT	32	52	31	33					
CONECT	33	53	32	34					
CONECT	34	54	33	35					
CONECT	35	55	16	34					
CONECT	36	4							
CONECT	37	8							
CONECT	38	8							
CONECT	39	8							
CONECT	40	11							
CONECT	41	12							
CONECT	42	12							
CONECT	43	13							
CONECT	44	14							
CONECT	45	20							
CONECT	46	21							
CONECT	47	22							
CONECT	48	23							
CONECT	49	27							
CONECT	50	27							
CONECT	51	7							
CONECT	52	32							
CONECT	53	33							
CONECT	54	34							
CONECT	55	35							
CONECT	56	9							
CONECT	57	9							
CONECT	58	10							
CONECT	59	10							
CONECT	60	10							
CONECT	61	9							
MASTER		0	0	0	0	0	0	0	0
END									

Coordinates of staurosporine in coo-file format (correct configuration)

The coordinates of staurosporine **3** in a coo-file format generated as an input for the program COSMOS with the correct configuration is given below.

```
$COO006
CELL 1.0000 1.0000 1.0000 90.000 90.000 90.000 0.0000 -0.7736 0.3485
NAME
SPGROUP 4
OPERATION CFF geometry optimization
ENERGY 1746.24
FORCE_FIELD_ENERGIES BondEn=20.0897 AngleEn=524.996 TorsionEn=968.372
PiTorsionEn=2.24663 CoulombEn=154.058 VdWEn=76.4751
ATOMS 61
HNMeB 1 11.53862 2.46940 3.28352 mb 1 0 40 0 0 0 0 0 0 0
HOMeB 1 6.77338 3.48126 2.57187 mb 1 0 38 0 0 0 0 0 0 0
HOMeA 1 5.75423 2.61411 1.41077 mb 1 0 38 0 0 0 0 0 0 0
HOMeC 1 7.35669 1.98770 1.80293 mb 1 0 38 0 0 0 0 0 0 0
O1 8 9.89456 6.35378 1.02193 mb 1 0 36 32 0 0 0 0 0 0
O5 8 11.71177 5.93743 8.47396 mb 1 1 19 0 0 0 0 0 0 0
O3p 8 7.31311 3.65458 0.51115 mb 1 0 38 33 0 0 0 0 0 0
N6 7 9.39828 6.03353 8.61005 mb 1 4 46 20 19 0 0 0 0 0
N12 7 8.08577 5.88667 2.70548 mb 1 6 32 29 28 0 0 0 0 0
N13 7 11.34322 5.71635 2.95222 mb 1 6 36 31 30 0 0 0 0 0
N4 7 9.57722 2.92385 2.52835 mb 1 0 61 40 34 0 0 0 0 0
C1 6 13.89846 5.41126 2.95766 mb 1 6 42 31 13 0 0 0 0 0
C2 6 15.03401 5.31352 3.80607 mb 1 6 43 14 12 0 0 0 0 0
C3 6 14.90378 5.37623 5.21389 mb 1 6 44 15 13 0 0 0 0 0
C4 6 13.63880 5.53381 5.82603 mb 1 6 45 16 14 0 0 0 0 0
Ca4 6 12.46744 5.63434 4.99486 mb 1 7 31 17 15 0 0 0 0 0
C4b 6 11.04300 5.78521 5.27124 mb 1 7 30 18 16 0 0 0 0 0
C4c 6 10.23506 5.89282 6.49702 mb 1 7 21 19 17 0 0 0 0 0
C5 6 10.55226 5.95316 7.92334 mb 1 7 18 8 6 0 0 0 0 0
```

C7	6	8.19571	6.02202	7.75381	mb	1	0	48	47	21	8	0	0	0	0
C7a	6	8.80035	5.95702	6.37238	mb	1	5	22	20	18	0	0	0	0	0
C7b	6	8.16582	5.93493	5.07192	mb	1	7	29	23	21	0	0	0	0	0
C7c	6	6.77588	5.93943	4.66485	mb	1	7	28	24	22	0	0	0	0	0
C8	6	5.57648	5.95609	5.46090	mb	1	6	49	25	23	0	0	0	0	0
C9	6	4.32782	5.94730	4.80575	mb	1	6	50	26	24	0	0	0	0	0
C10	6	4.27318	5.91276	3.39523	mb	1	6	51	27	25	0	0	0	0	0
C11	6	5.45218	5.87265	2.60168	mb	1	6	52	28	26	0	0	0	0	0
C11a	6	6.77022	5.90283	3.20691	mb	1	7	27	23	9	0	0	0	0	0
C12a	6	8.92992	5.88166	3.82671	mb	1	7	30	22	9	0	0	0	0	0
C12b	6	10.39241	5.80508	3.95652	mb	1	7	29	17	10	0	0	0	0	0
C13a	6	12.59214	5.58143	3.54744	mb	1	7	16	12	10	0	0	0	0	0
C2p	6	8.56110	5.77270	1.24056	mb	1	0	37	33	9	5	0	0	0	0
C3p	6	8.59718	4.33755	0.61086	mb	1	0	53	34	32	7	0	0	0	0
C4p	6	9.75972	3.43772	1.13198	mb	1	0	54	35	33	11	0	0	0	0
C5p	6	11.07816	4.21886	0.88642	mb	1	0	56	55	36	34	0	0	0	0
C6p	6	11.08000	5.64643	1.48341	mb	1	0	57	35	10	5	0	0	0	0
C_CH3	6	7.69127	6.70084	0.34794	mb	1	0	60	59	58	32	0	0	0	0
COMe	6	6.78839	2.91377	1.63405	mb	1	0	3	4	2	7	0	0	0	0
HNMeC	1	10.19885	1.67718	4.13704	mb	1	0	40	0	0	0	0	0	0	0
CNMe	6	10.55529	1.99528	3.14603	mb	1	0	1	41	11	39	0	0	0	0
HNMea	1	10.68683	1.09309	2.53037	mb	1	0	40	0	0	0	0	0	0	0
H1	1	14.02724	5.35864	1.88623	mb	1	0	12	0	0	0	0	0	0	0
H2	1	16.01431	5.18968	3.36817	mb	1	0	13	0	0	0	0	0	0	0
H3	1	15.78691	5.30144	5.83253	mb	1	0	14	0	0	0	0	0	0	0
H4	1	13.56981	5.57471	6.90182	mb	1	0	15	0	0	0	0	0	0	0
H6	1	9.35233	6.08980	9.64007	mb	1	0	8	0	0	0	0	0	0	0
H7b	1	7.59713	6.93464	7.89570	mb	1	0	20	0	0	0	0	0	0	0
H7a	1	7.57474	5.13756	7.96316	mb	1	0	20	0	0	0	0	0	0	0
H8	1	5.61400	5.97175	6.53962	mb	1	0	24	0	0	0	0	0	0	0
H9	1	3.41441	5.96374	5.38356	mb	1	0	25	0	0	0	0	0	0	0
H10	1	3.30828	5.91062	2.90785	mb	1	0	26	0	0	0	0	0	0	0
H11	1	5.30049	5.80408	1.53902	mb	1	0	27	0	0	0	0	0	0	0
H3p	1	8.84394	4.51151	-0.44933	mb	1	0	33	0	0	0	0	0	0	0

H4p	1	9.79422	2.54025	0.49306	mb	1	0	34	0	0	0	0	0	0	0	0
H5pb	1	11.19706	4.32689	-0.20425	mb	1	0	35	0	0	0	0	0	0	0	0
H5pa	1	11.95853	3.64714	1.21727	mb	1	0	35	0	0	0	0	0	0	0	0
H6p	1	11.92192	6.18268	1.01942	mb	1	0	36	0	0	0	0	0	0	0	0
HMeB	1	8.11947	6.78564	-0.66322	mb	1	0	37	0	0	0	0	0	0	0	0
HMea	1	7.64650	7.72028	0.76100	mb	1	0	37	0	0	0	0	0	0	0	0
HMec	1	6.66739	6.34212	0.19925	mb	1	0	37	0	0	0	0	0	0	0	0
H_N4	1	9.45793	3.70706	3.17692	mb	1	0	11	0	9	0	0	0	0	0	0

Data file for MD simulation in program COSMOS for staurosporine 3

The cosmos data file (.cod) containing the experimental data for norcamphor prepared for the MDOC run in the program COSMOS is shown below. The file contains at the beginning lines with remarks (REMARK), which contains information about the conditions and the origin of data, the used groups and their meaning. The experimental RDCs used as constraints follow (DD_TENSORS), showing the used grouping (GROUP_MEMBERS), and fixing of the methylene protons (FIXED_DISTANCES).

Beginning of the COSMOS data file

```
$COD003
REMARK Staurosporine_.cod: modelling setup for the RDC constrained MD runs for 8
different Staurosporine starting coordinates:
REMARK SRRR, SRSR, SSRR, SSSR in chair and boat conformation
REMARK Dipolar 1 bond CH couplings and errors taken from
"ChemComm08_5722_Luy_dPS_Staurosporin_SI.pdf"
REMARK "Deuterated polymer gels for measuring anisotropic NMR parameters with
strongly reduced artefacts" by Grit Kummerloewe
REMARK Fixing: - for fixing all initial CH-bond distances during run, in Force
Field Options, set "group 5" in "MD:Fix Bonds Lengths in Group"
REMARK - for fixing (non-bond) distances in between geminal protons and to
second neighbours , set "group 8" in "MD:Fix Distances for Group"
REMARK - for fixing all atoms to second neighbours, apply python script on coo-
File
REMARK Version: 1.0
RC_OPT_MOLECULE IN_MOL
RDC_OPT_MOLECULE IN_MOL
NAMES_OPT_FIT_TO EXACT
DATA_OPT_END
DD_TENSORS 13
H3p      C3p      9.90    9.90    19.8    0 0 0(5.0)
H4p      C4p      1.85    1.85    -3.7    0 0 0(1.0)
H5pa     C5p     -3.75   -3.75     7.5    0 0 0(3.2)
H6p      C6p     -2.90   -2.90     5.8    0 0 0(1.1)
C_CH3    C2p      1.60    1.60    -3.2    0 0 0(1.0)
H1       C1      13.60   13.60   -27.2    0 0 0(2.5)
H2       C2       5.55    5.55   -11.1    0 0 0(7.6)
H3       C3      -0.85   -0.85     1.7    0 0 0(4.2)
H4       C4      13.55   13.55   -27.1    0 0 0(1.0)
H8       C8      12.65   12.65   -25.3    0 0 0(1.0)
H9       C9       6.45    6.45   -12.9    0 0 0(5.4)
H10      C10     -1.30   -1.30     2.6    0 0 0(3.6)
H11      C11     12.70   12.70   -25.4    0 0 0(1.1)
FIXED_DISTANCES 4
H7[ab]   N6
```



```

H7[ab]  C7a
H7a      H7b
H5p[ab] C[46]p
GROUP_MEMBERS 23
C.*$      1 all Carbons
H.*$      2 all Protons
H[346]p    3 DDs
C_CH3      3
H5pa       3
H[1-489]   3
H1[01]     3
H.*$      5 Fix CH-bond
C[3-6]p    6 13C for RDC calculation3
[CH][1-489] 6
[CH][1][01] 6
O[13].*$   7 Torsion angles
C[2-6]p    7
N1[23]     7
N4         7
C_CH3      7
C12[ab]    7
C[ON]Me    7
N6         8 Fix distances of geminal protons
H7[ab]     8
C7a        8
C[46]p     8
H5p[ab]    8
END

```

End of COSMOS data file

.....

Oidiolactone B

Assignment data of Oidiolactone B

A total of 8.1 mg of solid Oidiolactone B was dissolved in 0.55 ml DMSO- d_6 , corresponding to a 48 mM isotropic solution. The NMR spectra needed for the assignment of Oidiolactone B are recorded on Bruker Avance II 600 MHz spectrometer equipped with a 5 mm BBI inversely detected 1H , ^{13}C double resonance probehead with actively shielded z-gradient. The respective frequencies are 600.19 MHz for proton, and 150.92 MHz for carbon. The temperature is controlled with Bruker VT-unit and is set to 300K. The homonuclear experiments used for the structure elucidation are the following: 1D 1H experiment and standard 2D COSY, TOCSY and NOESY together with their 1D selective versions (sel. TOCSY and sel. NOE) with various mixing times. Heteronuclear experiments applied for assignment and RDC-measurement have been: modified 1D ^{13}C experiment with a broadband BEBOP pulse for uniform excitation; a 2D CLIP-HSQC [4], a 2D P.E.HSQC [5], the HSQC-TOCSY-IP [6] and an HMBC. The aligned sample in PAN gel with 2.4 mm dry diameter of the polymer stick, irradiated with 440 kGy irradiation dose [7] consists of 12 mg analyte compound in 0.4 ml DMSO- d_6 .

Table S4. Experimental data of the assignment for Oidiolactone B in DMSO- d_6

Assignment	$\delta_{1H}/[ppm]$	$J_{HH}/[Hz]$	$\delta_{13C}/[ppm]$	Observed NOEs with
C1	-	-	162.42	
C2-H2	5.77 d	1.8	111.35	H5, w. H8, CH3-9, H10a, H10b
C3	-	-	157.38	
C4	-	-	132.48	
C5-H5	6.01 t	1.5	100.93	H2, H6, CH3-9, O-CH3
C6-H6	6.45 dt	4.6, 1.8	123.67	H5, H7, CH3-9, O-CH3
C7-H7	5.20 dt	4.8, 1.2	71.08	H6, H8, w. CH3-9, CH3-13
C8-H8	2.06 d	4.8	46.41	w. H2, H7, H12a, CH3-13
CH3-9	1.03 s	-	24.26	H2, H5, H6, H10b, H11*, H12b
C10-H10 α	1.60 m*	q#, 7.3#	29.09	H2, H11*
C10-H10 β	1.68 m*	t#, 6.7#	29.09	H2, CH3-9
C11-H11 α	1.65 m*	m#, 7.1#	16.97	*

C11-H11 β	1.65 m*	m#, 7.1#	16.97	*
C12-H12 α	1.45 m	dd#, 7.0#, 6.7#	27.35	H8, CH3-13
C12-H12 β	2.02 m	dd#, 7.3#, 5.4#	27.35	CH3-9, w. CH3-13
CH3-13	1.24 s	-	23.55	H7, H8, H11, H12a, w. H12b
C14	-	-	180.90	
O-CH3	3.59 s	-	56.70	H5, H6, H7

*- marks partially or fully overlapping signals. # indicates that multiplicity and the extracted coupling constants are derived from a P.E.HSQC experiment in isotropic solution.

Experimental data for Oidiolactone B in PAN/DMSO-d₆

Table S5. Experimental data for Oidiolactone B in PAN/DMSO-d₆ measured on a Bruker Avance II 600 MHz spectrometer at 300 K

Assignment	$\delta_{1H}/[\text{ppm}]$	$\delta_{13C}/[\text{ppm}]$	$^1T_{CH}/[\text{Hz}]$	$^1D_{CH}/[\text{Hz}]$	Error [Hz]
C2-H2	5.77	111.35	160.45	-10.42	± 0.4
C5-H5	6.01	100.93	177.68	5.77	± 0.4
C6-H6	6.45	123.67	157.99	-10.13	± 2.0
C7-H7	5.20	71.08	153.37	-0.76	± 0.4
C8-H8	2.06	46.41	155.92	18.15	± 1.0
CH3-9	1.03	24.26	123.35	-4.70	± 1.0
C10-H10 α	1.60	29.09	143.23	15.57	± 1.5
C10-H10 β	1.68	29.09	127.45	-1.26	± 1.0
C11-H11 α	1.65 *	16.97	128.84	0.52	± 2.5
C11-H11 β	1.65 *	16.97	130.83	0.76	± 2.5
C12-H12 α	1.45	27.35	128.41	-0.33	± 1.0
C12-H12 β	2.02	27.35	138.78	10.26	± 1.5
CH3-13	1.24	23.55	129.78	0.42	± 0.2
O-CH3	3.59	56.7	146.98	2.81	± 0.4

*- marks partially or fully overlapping signals

Coordinates of Oidiolactone B in pdb file format

The coordinates of the Oidiolactone B **4** in a pdb-file format generated as an output from the program COSMOS with the correct configuration and a starting boat conformation is given below. This configuration is marked as *Ref* throughout the manuscript.

```
HEADER      NO HEADER DEFINED AND DEFAULT DATE USED          01-JAN-00
AUTHOR      PDB FILE FORMAT GENERATED BY COSMOS
COMPND      UNNAMED
REMARK      CREATED FILE CONTAINS ONLY BASIC MOLECULAR DATA
REMARK CELL 1.0000 1.0000 1.0000 90.000 90.000 90.000 0.0000 0.0000
0.0000
REMARK SPGROUP P1
REMARK SOURCE PDB: NO HEADER DEFINED AND DEFAULT DATE USED 01-JAN-00
CRYST1      1.000    1.000    1.000  90.00  90.00  90.00 P 1          1
ATOM        1  O14  A   A   1      2.149   4.162   2.097   1.00   0.00          O
ATOM        2  O1   A   A   1     -2.595   5.936  -0.905   1.00   0.00          O
ATOM        3  O14 NOP A   1      3.130   3.964   4.154   1.00   0.00          O
ATOM        4  O5   NOP A   1     -0.475   5.865  -1.911   1.00   0.00          O
ATOM        5  O1   NOP A   1     -4.610   6.160   0.088   1.00   0.00          O
ATOM        6  C13 CH3 A   1      1.065   1.613   3.792   1.00   0.00          C
ATOM        7  C5   CH3 A   1     -0.774   6.790  -2.947   1.00   0.00          C
ATOM        8  C9   CH3 A   1      0.046   6.167   3.302   1.00   0.00          C
ATOM        9  C10 NOP A   1     -1.771   4.635   4.122   1.00   0.00          C
ATOM       10  C11 NOP A   1     -1.176   3.741   5.224   1.00   0.00          C
ATOM       11  C12 NOP A   1      0.344   3.582   5.190   1.00   0.00          C
ATOM       12  C13 NOP A   1      0.858   3.137   3.811   1.00   0.00          C
ATOM       13  C8   NOP A   1     -0.042   3.598   2.663   1.00   0.00          C
ATOM       14  C9   NOP A   1     -0.815   4.926   2.933   1.00   0.00          C
ATOM       15  C3   NOP A   1     -1.514   5.302   1.614   1.00   0.00          C
ATOM       16  C4   NOP A   1     -0.671   5.288   0.419   1.00   0.00          C
ATOM       17  C6   NOP A   1      0.484   4.594   0.400   1.00   0.00          C
ATOM       18  C7   NOP A   1      0.937   3.699   1.508   1.00   0.00          C
ATOM       19  C14 NOP A   1      2.172   3.793   3.418   1.00   0.00          C
ATOM       20  C2   NOP A   1     -2.795   5.678   1.485   1.00   0.00          C
ATOM       21  C1   NOP A   1     -3.405   5.962   0.175   1.00   0.00          C
ATOM       22  C5   NOP A   1     -1.194   6.153  -0.709   1.00   0.00          C
ATOM       23  H10 C10 b   1     -2.113   5.578   4.571   1.00   0.00          H
ATOM       24  H10 C10 a   1     -2.681   4.132   3.769   1.00   0.00          H
ATOM       25  H11 C11 a   1     -1.627   2.743   5.138   1.00   0.00          H
ATOM       26  H11 C11 b   1     -1.484   4.121   6.206   1.00   0.00          H
ATOM       27  H12 C12 a   1      0.633   2.852   5.958   1.00   0.00          H
ATOM       28  H12 C12 b   1      0.818   4.512   5.518   1.00   0.00          H
ATOM       29  H3   C13 C   0      1.477   1.261   2.840   1.00   0.00          H
ATOM       30  H2   C13 C   0      0.121   1.085   3.965   1.00   0.00          H
ATOM       31  H1   C13 C   0      1.772   1.305   4.571   1.00   0.00          H
ATOM       32  H2   C2   A   1     -3.481   5.743   2.321   1.00   0.00          H
ATOM       33  H5   C5   A   1     -1.037   7.210  -0.449   1.00   0.00          H
ATOM       34  H3   C5   C   0     -0.171   6.530  -3.821   1.00   0.00          H
ATOM       35  H2   C5   C   0     -0.517   7.809  -2.641   1.00   0.00          H
ATOM       36  H1   C5   C   0     -1.830   6.735  -3.227   1.00   0.00          H
```

ATOM	37	H6	C6	A	1	1.124	4.628	-0.479	1.00	0.00	H
ATOM	38	H7	C7	A	1	1.135	2.710	1.076	1.00	0.00	H
ATOM	39	H8	C8	A	1	-0.789	2.824	2.428	1.00	0.00	H
ATOM	40	H2	C9	C	0	-0.587	7.061	3.384	1.00	0.00	H
ATOM	41	H1	C9	C	0	0.812	6.397	2.554	1.00	0.00	H
ATOM	42	H3	C9	C	0	0.558	6.076	4.260	1.00	0.00	H
CONNECT	1	18	19								
CONNECT	2	21	22								
CONNECT	3	19									
CONNECT	4	22	7								
CONNECT	5	21									
CONNECT	6	29	30	31	12						
CONNECT	6										
CONNECT	7	4	34	35	36						
CONNECT	7										
CONNECT	8	40	41	42	14						
CONNECT	8										
CONNECT	9	23	24	10	14						
CONNECT	9										
CONNECT	10	9	25	26	11						
CONNECT	10										
CONNECT	11	10	27	28	12						
CONNECT	11										
CONNECT	12	6	11	13	19						
CONNECT	12										
CONNECT	13	12	39	14	18						
CONNECT	13										
CONNECT	14	8	9	13	15						
CONNECT	14										
CONNECT	15	14	16	20							
CONNECT	16	15	17	22							
CONNECT	17	16	37	18							
CONNECT	18	1	13	17	38						
CONNECT	18										
CONNECT	19	1	3	12							
CONNECT	20	15	32	21							
CONNECT	21	2	5	20							
CONNECT	22	2	4	16	33						
CONNECT	22										
CONNECT	23	9									
CONNECT	24	9									
CONNECT	25	10									
CONNECT	26	10									
CONNECT	27	11									
CONNECT	28	11									
CONNECT	29	6									
CONNECT	30	6									
CONNECT	31	6									
CONNECT	32	20									
CONNECT	33	22									
CONNECT	34	7									
CONNECT	35	7									
CONNECT	36	7									
CONNECT	37	17									
CONNECT	38	18									

CONECT	39	13												
CONECT	40	8												
CONECT	41	8												
CONECT	42	8												
MASTER		0	0	0	0	0	0	0	0	42	0	42	0	
END														

Coordinates of Oidiolactone B in coo-file format

The coordinates of Oidiolactone B **4** in a coo-file format generated as an input for the program COSMOS with the correct configuration is given below.

```
$COO006
CELL 1.0000 1.0000 1.0000 90.000 90.000 90.000 0.0000 0.0000 0.0000
NAME UNNAMED
SPGROUP P1
SOURCE PDB: NO HEADER DEFINED AND DEFAULT DATE USED 01-JAN-00
ATOMS 42
O1_a 8 -2.59528 5.93578 -0.90511 mb 1 0 10 9 0 0 0 0 0 0
O14_a 8 2.14968 4.16170 2.09650 mb 1 0 13 12 0 0 0 0 0 0
O1 8 -4.61038 6.16091 0.08793 mb 1 1 10 0 0 0 0 0 0 0
O5 8 -0.47512 5.86524 -1.91100 mb 1 0 9 7 0 0 0 0 0 0
O14 8 3.13045 3.96351 4.15361 mb 1 1 12 0 0 0 0 0 0 0
C9_CH3 6 0.04665 6.16757 3.30263 mb 1 0 42 41 40 17 0 0 0 0
C5_CH3 6 -0.77400 6.78989 -2.94726 mb 1 0 35 34 33 4 0 0 0 0
C13_CH3 6 1.06473 1.61261 3.79161 mb 1 0 31 30 29 19 0 0 0 0
C5 6 -1.19444 6.15327 -0.70878 mb 1 0 36 15 4 1 0 0 0 0
C1 6 -3.40492 5.96237 0.17470 mb 1 3 11 3 1 0 0 0 0 0
C2 6 -2.79500 5.67765 1.48435 mb 1 6 32 16 10 0 0 0 0 0
C14 6 2.17205 3.79258 3.41782 mb 1 2 19 5 2 0 0 0 0 0
C7 6 0.93653 3.69866 1.50788 mb 1 0 38 18 14 2 0 0 0 0
C6 6 0.48363 4.59406 0.40039 mb 1 2 37 15 13 0 0 0 0 0
C4 6 -0.67172 5.28885 0.41842 mb 1 3 16 14 9 0 0 0 0 0
C3 6 -1.51359 5.30207 1.61473 mb 1 6 17 15 11 0 0 0 0 0
C9 6 -0.81467 4.92563 2.93405 mb 1 0 22 18 16 6 0 0 0 0
C8 6 -0.04190 3.59785 2.66347 mb 1 0 39 19 17 13 0 0 0 0
C13 6 0.85835 3.13655 3.81122 mb 1 0 20 18 12 8 0 0 0 0
C12 6 0.34356 3.58107 5.19050 mb 1 0 28 27 21 19 0 0 0 0
C11 6 -1.17606 3.74056 5.22492 mb 1 0 26 25 22 20 0 0 0 0
```


C10_6 -1.77104 4.63467 4.12254 mb 1 0 24 23 21 17 0 0 0 0
H10_C10_a 1 -2.68089 4.13178 3.76918 mb 1 0 22 0 0 0 0 0 0 0
H10_C10_b 1 -2.11237 5.57796 4.57135 mb 1 0 22 0 0 0 0 0 0 0
H11_C11_b 1 -1.48414 4.12059 6.20576 mb 1 0 21 0 0 0 0 0 0 0
H11_C11_a 1 -1.62685 2.74285 5.13723 mb 1 0 21 0 0 0 0 0 0 0
H12_C12_b 1 0.81820 4.51160 5.51769 mb 1 0 20 0 0 0 0 0 0 0
H12_C12_a 1 0.63333 2.85163 5.95736 mb 1 0 20 0 0 0 0 0 0 0
H1_C13_CH3 1 1.77202 1.30416 4.57038 mb 1 0 8 0 0 0 0 0 0 0
H2_C13_CH3 1 0.12072 1.08499 3.96455 mb 1 0 8 0 0 0 0 0 0 0
H3_C13_CH3 1 1.47759 1.26068 2.84012 mb 1 0 8 0 0 0 0 0 0 0
H2_C2 1 -3.48162 5.74330 2.32019 mb 1 0 11 0 0 0 0 0 0 0
H1_C5_CH3 1 -1.82939 6.73490 -3.22785 mb 1 0 7 0 0 0 0 0 0 0
H2_C5_CH3 1 -0.51698 7.80866 -2.64129 mb 1 0 7 0 0 0 0 0 0 0
H3_C5_CH3 1 -0.17173 6.52957 -3.82162 mb 1 0 7 0 0 0 0 0 0 0
H5_C5 1 -1.03735 7.21007 -0.44872 mb 1 0 9 0 0 0 0 0 0 0
H6_C6 1 1.12364 4.62755 -0.47928 mb 1 0 14 0 0 0 0 0 0 0
H7_C7 1 1.13514 2.70995 1.07651 mb 1 0 13 0 0 0 0 0 0 0
H8_C8 1 -0.78939 2.82440 2.42821 mb 1 0 18 0 0 0 0 0 0 0
H3_C9_CH3 1 0.55792 6.07605 4.26072 mb 1 0 6 0 0 0 0 0 0 0
H1_C9_CH3 1 0.81200 6.39683 2.55427 mb 1 0 6 0 0 0 0 0 0 0
H2_C9_CH3 1 -0.58676 7.06036 3.38353 mb 1 0 6 0 0 0 0 0 0 0

Data file for COSMOS MD simulation (.cod) for oidiolactone B (4)

The cosmos data file (.cod) containing the experimental data for oidiolactone B **4** prepared for the MDOC run in the program COSMOS is shown below. The file contains at the beginning lines with remarks (REMARK), which contains information about the conditions and the origin of data, the used groups and their meaning. The experimental RDCs used as constraints follow (DD_TENSORS), showing the used grouping (GROUP_MEMBERS), and fixing of the methylene protons (FIXED_DISTANCES).

Beginning of the COSMOS data file

```
$COD003
REMARK NMR parameters for Oidiolactone B
REMARK Oidiolactone B in PAN and DMSO-d6
REMARK RDC from alignment with different stretching, here delta nu_Q=11 Hz,
clipHSQC data
REMARK Group 1: all Carbons
REMARK Group 2: all protons
REMARK Group 3: bond DD tensors - used as constraints (both atoms have to be in
group 1)
REMARK Group 4: RDC values - used as constraints (both atoms have to be in group
4)
REMARK Group 5: fixed distances
REMARK Group 6: 13C for RDC calculation
REMARK Group 7: Torsion angles for Mathematica snapshot
REMARK ordered exp. Values
RC_OPT_MOLECULE IN_MOL
RDC_OPT_MOLECULE IN_MOL
NAMES_OPT_FIT_TO EXACT
DATA_OPT_END
DD_TENSORS 14
H2_C2      C2      5.21      5.21 -10.42  0      0      0(0.4)
H5_C5      C5      -2.89      -2.89  5.77   0      0      0(0.4)
H6_C6      C6      5.07      5.07 -10.13  0      0      0(2.0)
H7_C7      C7      0.38      0.38 -0.76   0      0      0(0.4)
H8_C8      C8      -9.08      -9.08 18.15  0      0      0(1.0)
C9_CH3     C9      2.35      2.35 -4.70   0      0      0(1.0)
H10_C10_a  C10     -7.79      -7.79 15.57  0      0      0(1.5)
H10_C10_b  C10      0.63      0.63 -1.26   0      0      0(1.0)
H11_C11_a  C11     -0.26      -0.26  0.52   0      0      0(2.5)
H11_C11_b  C11     -0.38      -0.38  0.76   0      0      0(2.5)
H12_C12_a  C12      0.17      0.17 -0.33   0      0      0(1.0)
H12_C12_b  C12     -5.13      -5.13 10.26  0      0      0(1.5)
C13_CH3    C13     -0.21      -0.21  0.42   0      0      0(0.2)
C5_CH3     O5      -1.41      -1.41  2.81   0      0      0(0.4)
GROUP_MEMBERS 20
^C.*$      1 all Carbons
^H.*$      2 all Protons
H[2-8]_C[2-8]  3 DD tensor (constraints)
H1[0-2]_C1[0-2]_*  3
```

C[59]_CH3	3
C13_CH3	3
H[2-8]_C[2-8]	4 RDC values
C[2-8]	4
H1[0-2]_C1[0-2]_.*	4
C1[0-3]	4
H[2-8]_.*_C[2-8]_.*	5 Atoms for fixed distances
^C[2-9]	6 13C for RDC calc
C1[0-3]	6
H[2567]_C[2-9]	7 tors angles
C[2-9]	7
H1[0-2]_C1[0-2]_.*	7
C1[0-3]	7
H1[0-2]_C1[0-2]_.*	8 Atoms for fixed distances
C1[0123]	8
C9	8
FIXED_DISTANCES 6	
H10_C10_.* C11	
H10_C10_.* C9	
H11_C11_.* C10	
H11_C11_.* C12	
H12_C12_.* C11	
H12_C12_.* C13	
END	

End of COSMOS data file

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