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Supporting Information

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Residual Chemical Shift Anisotropy (RCSA): A Tool for the Analysis of the Configuration of Small Molecules**

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Supporting Information

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Full Reference for Gaussian 03

Gaussian 03, Revision C.02,
M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, and J. A. Pople,
Gaussian, Inc., Wallingford CT, 2004.

Materials and Sample Preparation

All chemicals were purchased from Sigma-Aldrich and were used without further purification. Solvents had p.a. grade and estrone of 99 % purity.

Gel-polymer (APS) Synthesis

(*S*)-2-aminopropanesulfonic acid (precursor of the APS monomer) was synthesized from the corresponding (*S*)-*β*-aminoalcohol by reaction with di-*tert*-butyldicarbonate [S1], followed by mesylation, Boc-deprotection and subsequent sulfonation according to literature [S2].

APS monomer: 3.5 g of (*S*)-2-aminopropanesulfonic acid (25 mmol) and 6.0 g of NaOH (150 mmol) were dissolved in 50 mL of water. To this solution 6.1 mL of acryloyl chloride (75 mmol) was added dropwise during 1 h while the reaction temperature was maintained at 0°C. After addition was completed, stirring was continued for additional 1 h at room temperature. The resulting solution was passed through a column of Dowex 50WX8 (H^+form) eluted with water. The eluate was evaporated to dryness under reduced pressure and the residue was crystallized from ethanol to give APS (4.3 g; yield 89%).

(*S*)-2-acrylamido-1-propanesulfonic acid: $[\alpha]_D^{25}$ = +6.0 (*c* = 1.0, MeOH); ^{1}H NMR (400 MHz, [D_6]DMSO, 25°C): δ = 1.18 (d, ^3J(H,H) = 6.6 Hz, 3H; CH_3), 2.58 (dd, ^3J(H,H) = 7.8 Hz, ^2J(H,H) = 13.5 Hz, 1H; CH_2), 2.75 (dd, ^3J(H,H) = 5.1 Hz, ^2J(H,H) = 13.5 Hz, 1H; CH_2), 4.10 (m, 1H; CH), 5.52 (dd, ^3J(H,H) = 10.1 Hz, ^2J(H,H) = 2.4 Hz, 1H; CH_2=CH), 6.01 (dd, ^2J(H,H) = 2.4 Hz, ^3J(H,H) = 17.1 Hz, 1H; CH_2=CH), 6.13 (dd, ^3J(H,H) = 10.1 Hz, ^3J(H,H) = 17.1 Hz, 1H; CH_2=*CH*), 8.01 ppm (NH); ^{13}C NMR (100 MHz, [D_6]DMSO, 25°C): δ = 20.2 (CH_3), 42.3 (CH), 56.5 (CH_2), 125.4 (CH_2=CH), 131.9 (CH_2=*CH*), 164.0 ppm (C=O); MS (ESI): *m/z* (%): 192.0 (100) $[M-H]^-$; HRMS (ESI): *m/z*: calcd for $C_6H_{11}NO_4S$ $[M-H]^-$: 192.03360; found: 192.03360.

Gel sample Preparation

APS gel: (*S*)-2-Acrylamido-1-propanesulfonic acid (APS), *N,N*-dimethylacrylamide (DMAA) and *N,N'*-methylenebisacrylamide (BIS) and ammonium persulfate (1:1:0.03:0.008) were dissolved in purified water to a total monomer concentration of 1.2 mol L^{-1} followed by devolatilization in vacuum for a few minutes. The pre-gel solution was inserted into a gel cylinder with an inner diameter of 7 mm and polymerized for 12 min at 70 °C. The gels were washed once with aqueous HCl (0.02 M), at least three times with water (each time for several hours) and finally dried at 30-40 °C.

In order to record NMR spectra at different degrees of alignment, the Kuchel stretching apparatus was used. Firstly, a flexible silicone rubber tube was inserted into an open-bottom 5 mm NMR glass tube. Secondly the dried APS stick was placed on the bottom of the silicone tube and this was closed on the bottom by a Teflon plug. Finally, 30 mg of estrone in 0.5 mL DMSO-d_6 solution was poured into the silicon tube. To avoid the formation of bubbles in the interface gel-solution it was necessary to carefully hit the NMR tube. Within fifteen days the gel was swollen. This swelling process was monitored by measuring the deuterium quadrupolar splitting of the solvent signal. When the splitting of the deuterium signal kept constant the ^{13}C and HSQC spectra were recorded before stretching. After the acquisition the silicon tube was stretched to an extension factor of 1.6 (the difference in length between the stretched and unstretched gel divided by the length of the unstretched gel) and fixed by using plastic clamps and screws and ^{13}C and HSQC spectra were recorded again.

NMR Analysis

All NMR spectra of estrone were recorded at 298 K in DMSO-d_6, and measured on a Bruker Avance III 600 spectrometer with a nominal ^{1}H frequency of 600.25 MHz using a 5 mm probe, except ^{2}H NMR spectra. The ^{1}H NMR spectra were acquired using 16 k data points at a spectral width of 6.3 kHz, with 16 scans and a 1.2 s delay between transients. The proton decoupled ^{13}C NMR spectra were acquired using 64 k data points at a spectral width of 36 kHz, with 12000 scans, 1.5 s delay between transients and 50 dummy scans. A standard Bruker pulse sequence (hsqcetgpsisp2.2) was used for performing a coupled ^{1}H-^{13}C HSQC spectrum**.** The heteronuclear 2D spectra were recorded using 512 (t_1) x 8192 (t_2) data points, collecting 16 scans per increment with a relaxation delay of 2.0 s. The spectral widths in the F2 and F1 dimensions were 5.1 kHz and 24.1 kHz, respectively. The 2D spectra were processed with a cosine window function. 2D homonuclear correlated NOESY spectrum was recorded using 128 (t_1) × 2048 (t_2) data points, collecting 16 scans per increment, with spectral widths of 5 kHz. The relaxation delay was 3.0 s and mixing time was set to 1 s. The ^{2}H NMR spectra were recorded at 61.42 MHz on a Bruker Avance 400 spectrometer, using 8 k data points at a spectral width of 2.46 kHz, with 8 scans and a 2.0 s delay between transients.

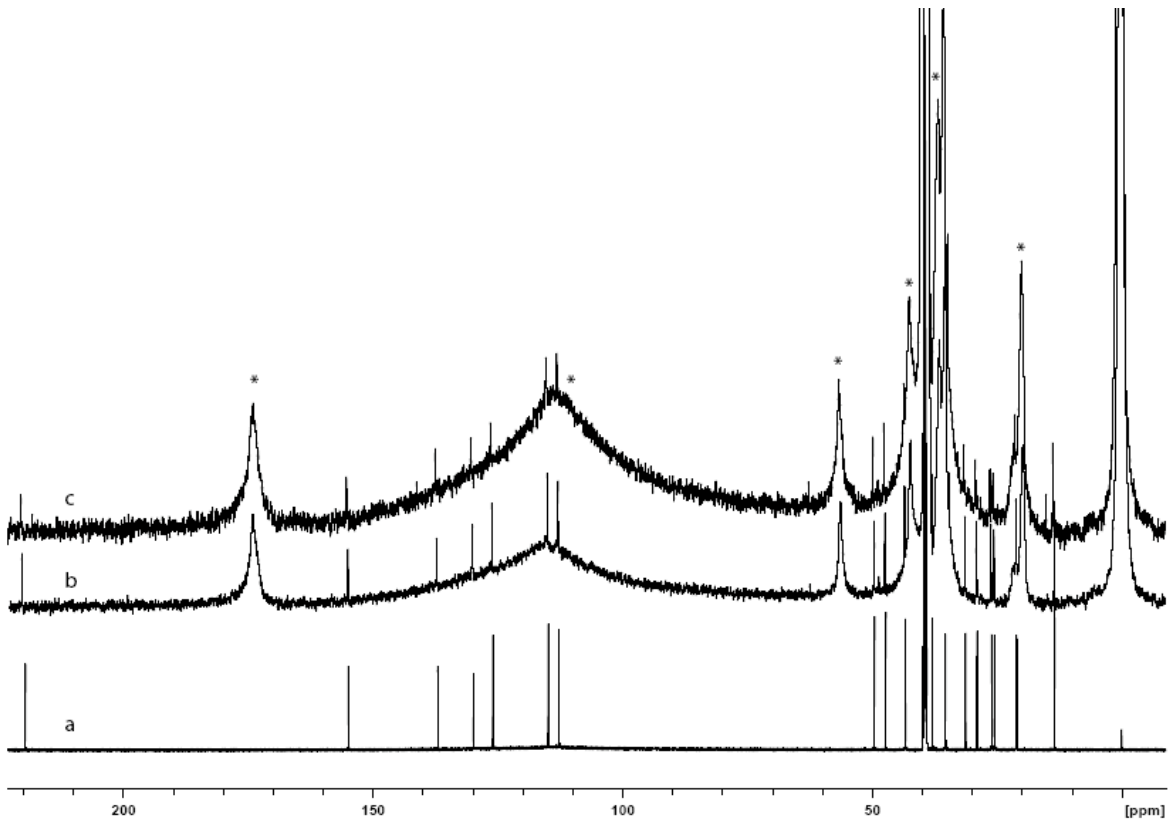

Figure S1. ^{13}C-{^{1}H} 150 MHz NMR spectra from estrone (a) isotropic solvent, (b) gel sample before stretching and (c) after stretching. The asterisk (*) corresponds to the gel signal.

The NMR signal assignment of estrone was based on HSQC and NOESY experiments and in comparison with literature data. [S3]

Estrone: ^{1}H NMR (600.25 MHz, [D$_6$]DMSO, 25°C): δ = 0.81 (s, 3H), 1.33 (m, 3H), 1.46 (m, 2H), 1.54 (m, 1H), 1.74 (m, 1H), 1.92 (m, 2H), 2.05 (dt, ^2J(H,H) = 18.8 Hz, ^3J(H,H) = 9.0 Hz, 1H), 2.13 (m, 1H), 2.30 (m, 1H), 2.42 (dd, ^2J(H,H) = 18.8 Hz, ^3J(H,H) = 8.5 Hz, 1H), 2.75 (m, 2H), 6.45 (d, ^4J(H,H) = 2.4 Hz, 1H), 6.51 (dd, ^3J(H,H) = 8.3 Hz, ^4J(H,H) = 2.4 Hz, 1H), 7.04 (d, ^3J(H,H) = 8.3 Hz, 1H), 9.01 ppm (OH); ^{13}C NMR: (150.95 MHz, [D$_6$]DMSO, 25°C): δ = 13.41 (C18), 21.03 (C15), 25.46 (C11), 26.03 (C7), 28.95 (C6), 31.26 (C12), 35.27 (C16), 37.87 (C8), 43.34 (C9), 47.22 (C13), 49.48 (C14), 1S12.69 (C2), 114.86 (C4), 125.95 (C1), 129.81 (C10), 137.00 (C5), 154.93 (C3), 219.58 ppm (C17).

SVD alignment tensor determination from RDCs and RCSAs

Following Losonczi et al. (S4) the alignment tensor can be determined from both RDCs D^i and RCSAs δ^m. The indices i and m are used to enumerate the respective anisotropic parameter. A is the alignment tensor.

$$D^i(Hz) = \frac{\kappa_i}{R_i^3}\left\langle \cos^2(\theta) - \frac{1}{3}\right\rangle_t = \frac{\kappa_i}{R_i^3}\begin{pmatrix} r_x^{kl} & r_y^{kl} & r_z^{kl}\end{pmatrix}\begin{pmatrix} A_{xx} & A_{xy} & A_{xz} \\ A_{xy} & A_{yy} & A_{yz} \\ A_{xz} & A_{yz} & A_{zz}\end{pmatrix}\begin{pmatrix} r_x^{kl} \\ r_y^{kl} \\ r_z^{kl}\end{pmatrix}$$

where $\kappa_i = -\frac{3}{8\pi^2}\gamma_k\gamma_l\mu_0\hbar$ being γ_k and γ_l the magnetogyric ratios for the coupled nuclei k and l

$\delta^m(Hz) = -\omega_m \sum_{ij=x,y,z} A_{ij}\sigma_{ij}^m$ being ω_m the Larmor frequency for nucleus m

$$\begin{pmatrix} \kappa_1\frac{(r_y^1)^2-(r_x^1)^2}{R_1^3} & \kappa_1\frac{(r_z^1)^2-(r_x^1)^2}{R_1^3} & \kappa_1\frac{2r_x^1r_y^1}{R_1^3} & \kappa_1\frac{2r_x^1r_z^1}{R_1^3} & \kappa_1\frac{2r_y^1r_z^1}{R_1^3} \\ . & . & . & . & . \\ \kappa_m\frac{(r_y^m)^2-(r_x^m)^2}{R_m^3} & \kappa_m\frac{(r_z^m)^2-(r_x^m)^2}{R_m^3} & \kappa_m\frac{2r_x^mr_y^m}{R_m^3} & \kappa_m\frac{2r_x^mr_z^m}{R_m^3} & \kappa_m\frac{2r_y^mr_z^m}{R_m^3} \\ . & . & . & . & . \\ . & . & . & . & . \\ -\omega_1(\sigma_{yy}^1-\sigma_{xx}^1) & -\omega_1(\sigma_{zz}^1-\sigma_{xx}^1) & -\omega_1(\sigma_{xy}^1+\sigma_{yx}^1) & -\omega_1(\sigma_{xz}^1+\sigma_{zx}^1) & -\omega_1(\sigma_{yz}^1+\sigma_{zy}^1) \\ . & . & . & . & . \\ -\omega_n(\sigma_{yy}^n-\sigma_{xx}^n) & -\omega_n(\sigma_{zz}^n-\sigma_{xx}^n) & -\omega_n(\sigma_{xy}^n+\sigma_{yx}^n) & -\omega_n(\sigma_{xz}^n+\sigma_{zx}^n) & -\omega_n(\sigma_{yz}^n+\sigma_{zy}^n) \end{pmatrix}\begin{pmatrix} A_{yy} \\ A_{zz} \\ A_{xy} \\ A_{xz} \\ A_{yz}\end{pmatrix} = \begin{pmatrix} D^1 \\ . \\ D^m \\ . \\ . \\ \delta^1 \\ . \\ \delta^n\end{pmatrix}$$

Using least-squares SVD decomposition the RDCs and RCSAs are used to calculate the alignment tensor A.

The merit of the fit is expressed in terms of the quality factor Q as [S5]

$$Q = \sqrt{\frac{(D_1^{exp}-D_1^{calc})^2+\ldots+(D_m^{exp}-D_m^{calc})^2+(\delta_1^{exp}-\delta_1^{calc})^2+\ldots+(\delta_n^{exp}-\delta_n^{calc})^2}{D_1^2+\ldots D_m^2+\delta_1^2+\ldots+\delta_n^2}}$$

ΔΔRCSAs and ΔRDCs: Experimental and Back Calculated

Table S1. Experimental and back calculated ΔΔRCSAs and ΔRDCs measured for estrone in APS alignment media, using ΔΔRCSAs and ΔRDCs for the tensor determination (in brackets: errors)

	Experimental (*Hz*)	Back calculated estrone (*Hz*)	Back calculated 13-epi-estrone (*Hz*)
ΔΔRCSAs			
C-1	8.00 (2.26)	6.94 (0.75)	4.53 (0.75)
C-2	7.24 (2.26)	4.98 (0.60)	3.32 (0.60)
C-3	8.90 (2.56)	7.09 (1.21)	3.62 (1.21)
C-4	6.34 (2.26)	3.92 (0.45)	3.62 (0.45)
C-5	5.13 (2.56)	7.09 (0.91)	4.08 (0.75)
C-8 *(reference)*	0.00	-	-
C-9	-0.91 (0.91)	0.60 (0.15)	0.45 (0.15)
C-10	7.69 (3.17)	8.15 (1.36)	4.68 (1.36)
C-13	-2.72 (0.60)	-0.30 (0.15)	-1.36 (0.75)
C-14	-3.77 (0.75)	-0.91 (0.30)	-1.06 (0.30)
C-15	-1.51 (1.21)	-0.75 (0.30)	-1.21 (0.75)
C-17	5.88 (2.26)	7.84 (1.81)	2.11 (1.51)
C-18	1.21 (0.75)	0.91 (0.15)	1.21 (0.15)
ΔRDCs			
C1-H1	-6.80 (1.20)	-7.27 (1.20)	-8.96 (1.20)
C2-H2	-3.80 (1.80)	-3.29(1.84)	-4.49 (1.74)
C4-H4	-7.80 (2.10)	-7.84 (1.15)	-9.18 (1.16)
C9-H9	16.10 (5.00)	16.78 (4.54)	19.53 (4.21)
C12-H12$_{\beta}$	-10.20 (4.70)	-9.40 (4.54)	-7.50 (4.39)
C18-H18	-8.70 (1.80)	-6.05 (0.88)	-4.58 (1.78)
***Q*-factor**		**0.328 (0.063)**	**0.453 (0.049)**

Coupling constants and corresponding individual maximum error estimates (corresponding to roughly three times the standard deviation) have been extracted by shifting 1D slices of the 2D spectra as described in detail previously [S6]: After extraction of corresponding 1D-slices, α- and β-components of the multiplets were shifted relative to each other and the shift in Hz is taken as the coupling constant. For an error estimate, not the center of the signals was overlapped, but the left- and rightmost positions of overlap of the two multiplet components with special consideration of the flanks and feet of the signals of interest. We then took the average of the left- and rightmost shifts as the corresponding coupling and half their difference as the individual maximum error estimate.
Relative chemical shift values were extracted out of a 1D ^{13}C-spectrum in a similar manner, shifting the reference signal (C8) to overlap with the signal of interest. While the overlap of the center of the signals reflects the relative chemical shift, the overlap at the right and left flank allow the estimation of the maximum individual error.

Table S2. Experimental and back calculated ΔΔRCSAs measured for estrone in APS alignment media, using ΔΔRCSAs only for the tensor determination (in brackets: errors)

	Experimental (*Hz*)	Back calculated estrone (*Hz*)	Back calculated 13-*epi*-estrone (*Hz*)
ΔΔRCSAs			
C-1	8.00 (2.26)	7.55 (1.81)	7.85 (1.66)
C-2	7.24 (2.26)	5.13 (1.81)	5.43 (1.66)
C-3	8.90 (2.56)	8.15 (2.11)	6.94 (1.51)
C-4	6.34 (2.26)	5.59 (1.36)	6.79 (1.36)
C-5	5.13 (2.56)	8.00 (1.66)	6.79 (1.96)
C-8 *(reference)*	0.00	-	-
C-9	-0.91 (0.91)	0.30 (0.30)	0.75 (0.45)
C-10	7.69 (3.17)	9.06 (1.81)	8.76 (1.81)
C-13	-2.72 (0.60)	-1.06 (0.60)	-3.17 (1.06)
C-14	-3.77 (0.75)	-2.57 (0.75)	-2.57 (1.21)
C-15	-1.51 (1.21)	-1.36 (0.45)	-2.87 (0.75)
C-17	5.88 (2.26)	5.13 (2.11)	4.68 (1.96)
C-18	1.21 (0.75)	0.00 (0.75)	2.57 (0.60)
***Q*-factor**		**0.352 (0.057)**	**0.339 (0.056)**

To evaluate the impact of experimental error in the fitting we used a Monte Carlo bootstrapping procedure where 512 different initial data sets were generated using 512 gaussian distributions centered on each measured ΔRDCs and ΔΔRCSAs and using reported experimental errors as standard deviations. SVD fitting was performed for each set and back predicted values and quality factors *Q* were then averaged over the 512 different computations and the corresponding standard deviations were computed. The histograms for estrone and 13-*epi*-estrone are depicted in Figure S2. The average values (Q = 0.328 and Q = 0.453 for estrone and 13-*epi*-estrone, respectively) are indicated in the main text.

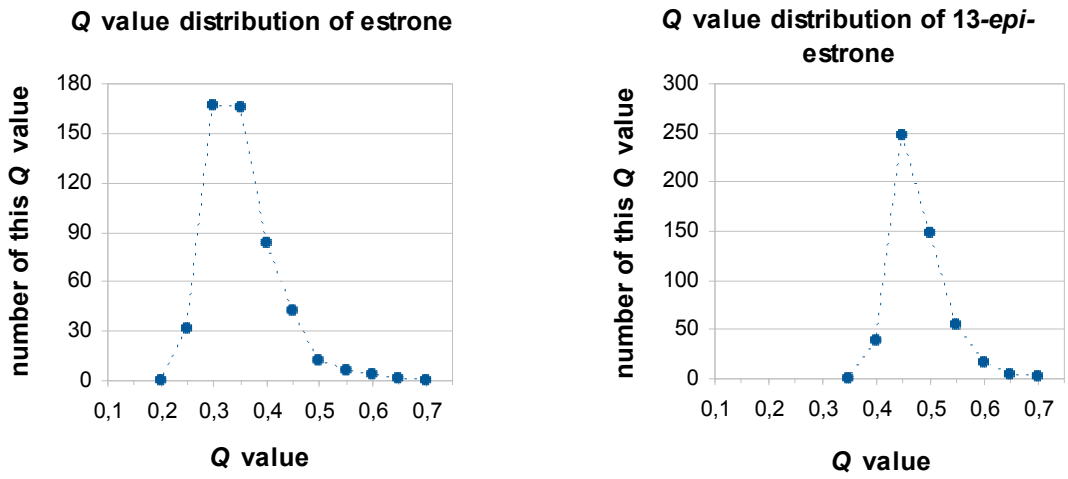

Figure S2: Histograms for the *Q* values for estrone and 13-*epi*-estrone obtained by bootstrapping.

Correlations between experimental and back calculated ΔΔRCSAs and ΔRDCs

Figure S3 shows the correlation between experimental ΔΔRCSAs and ΔRDCs, obtained by estrone, and back calculated ΔΔRCSAs and ΔRDCs of estrone and 13-*epi*-estrone using ΔΔRCSAs as well as ΔRDCs for determination of alignment tensor (data taken from Table S1). The back calculated values were obtained by implementing the experimental ΔΔRCSA and ΔRDC values into MSpin. The *Q*-values show that the ΔΔRCSAs and ΔRDCs together can reliably distinguish between the two configurations.

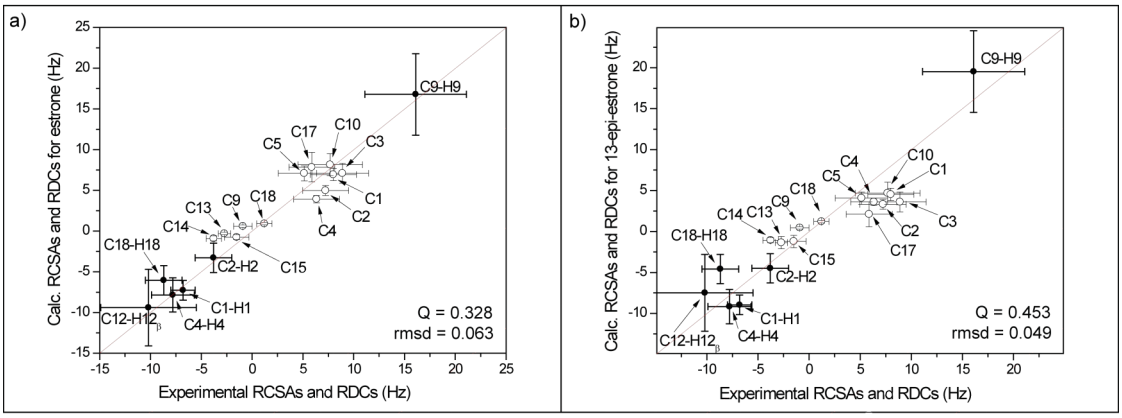

Figure S3. Correlation between the experimental and back-calculated ΔΔRCSAs (○) and ΔRDCs (●) for estrone (a) and 13-*epi*-estrone (b), tensor determination using experimental ΔΔRCSAs and ΔRDCs. $Q = 0.328$ and $Q = 0.453$ for estrone and 13-*epi*-estrone, respectively.

Correlations between experimental and back calculated ΔΔRCSAs

Figure S4 shows the correlation between experimental ΔΔRCSAs, obtained by estrone, and back calculated ΔΔRCSAs of estrone and 13-*epi*-estrone using only ΔΔRCSAs for determination of alignment tensor (data taken from Table S2). In this case the back calculated ΔΔRCSAs were obtained by implementing only the ΔΔRCSAs experimental values in MSpin. The *Q*-values show that the ΔΔRCSAs alone cannot reliably distinguish between the two configurations.

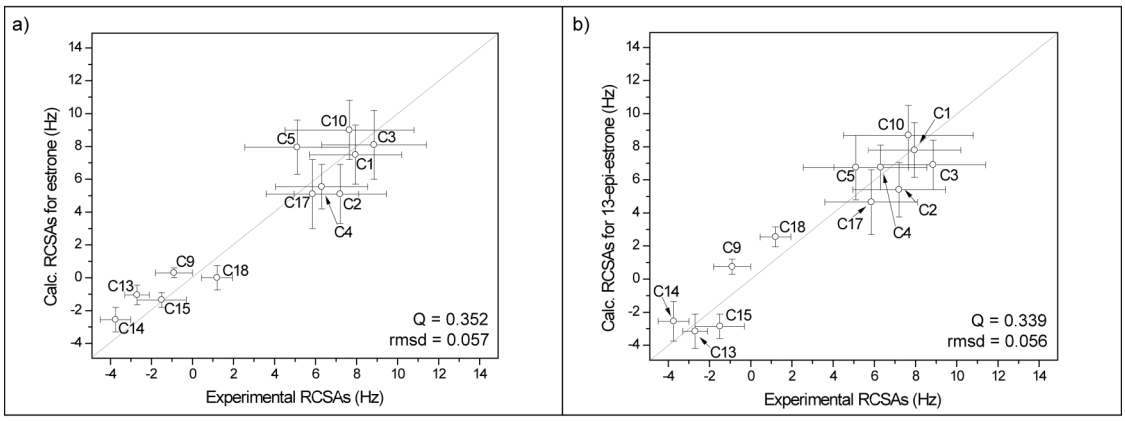

Figure S4. Correlation between the experimental and back-calculated ΔΔRCSAs for estrone (a) and 13-*epi*-estrone (b), tensor determination only with experimental ΔΔRCSAs. $Q = 0.352$ and $Q = 0.339$ for estrone and 13-*epi*-estrone, respectively.

Computational

Molecular Mechanics

Firstly, we did a conformational search based on molecular mechanics calculations for estrone and 13-*epi*-estrone. This was performed with Discovery Studio 2.5 (Accelrys) using the standard CFF force field for organic molecules [S7]. In the program we used the "generate conformations" protocol with the FAST search method [S8]. Using this random search method with poling to generate conformations, the molecule is split into pieces, a systematic search is performed on each piece, and the pieces are randomly reconnected. Each new conformation is optimized in the torsion space with poling penalty in order to maintain conformational diversity (Table S3). Within a 33 kJ mol^{-1} energy threshold two conformers of estrone and four conformers of 13-*epi*-estrone were found. In table S2 the total energies for each conformer are listed.

Table S3. Total energies of the conformations generated by molecular mechanics calculations.

	Conformation	Total Energy (kJ mol^{-1})
Estrone	1	118.14
	2	130.11
13-*epi*-estrone	1	122.09
	2	126.52
	3	140.11
	4	126.99

DFT Calculations

The geometries of the six conformations obtained by molecular mechanic calculations were optimized at the DFT level of theory, using Gaussian03 Revision C.02 (Frisch 2004). The B3LYP functional along with the 6-311+G(d) basis set was used. The calculated free energy differences between conformations were more than 9 kJ mol^{-1} indicating that only one conformer for each epimer is populated (Table S4).

Table S4. Relative Free Energies (kJ mol^{-1}) of the conformers calculated by DFT.

	Conformation	E (hartree)	ΔG (kJ mol^{-1})
Estrone	1	-849.49656	9.1
	2	-849.50002	0.0
13-*epi*-estrone	1	-849.50080	10.8
	2	-849.49839	17.1
	3	-849.49559	24.5
	4	-849.50492	0.0

To check the accuracy of the DFT chemical shift calculation we compared the experimental isotropic chemical shift with the calculated one. The ^{13}C chemical shift tensors calculations were carried out using the optimized structures by Gaussian03 as input coordinates, with the

B3LYP functional, 6-31+G(d) and 6-311+G(d) basis sets, and were done *in vacuo* using the IEFPCM solvent continuum model [S9] as implemented in Gaussian03 (DMSO as solvent). [S4] The calculated ^{13}C chemical shieldings were converted to chemical shifts using the equation

$$\delta_{calc} = \sigma_{TMS} - \sigma_{calc} \qquad \text{(S1)}$$

where δ_{calc} is the isotropic chemical shift from a particular nucleus *X*; σ_{TMS} and σ_{calc} correspond to the average of the four carbon chemical shieldings of TMS and the chemical shielding of the nucleus *X*.
Correlation coefficients and standard deviations (SD) of the fits between calculated and experimental data were obtained using Origin™ (Table S5 and Figure S5).

Table S5: Slopes, intercepts, correlation coefficients and standard deviations between experimental and calculated isotropic ^{13}C chemical shifts for estrone.

Basis set	*a**	*b**	Correlation coefficients	Standard deviation
estrone				
6-311+G(d) in vacuum	4.26	1.02	0.99959	1.808
6-311+G(d) in DMSO	2.99	1.04	0.99913	2.706
13-*epi*-estrone				
6-311+G(d) in vacuum	6.30	1.01	0.99856	3.340
6-311+G(d) in DMSO	5.15	1.04	0.99792	4.120

* $y = a + bx$

Incorporation of DMSO as solvent did not improve the correlation (Table S5).

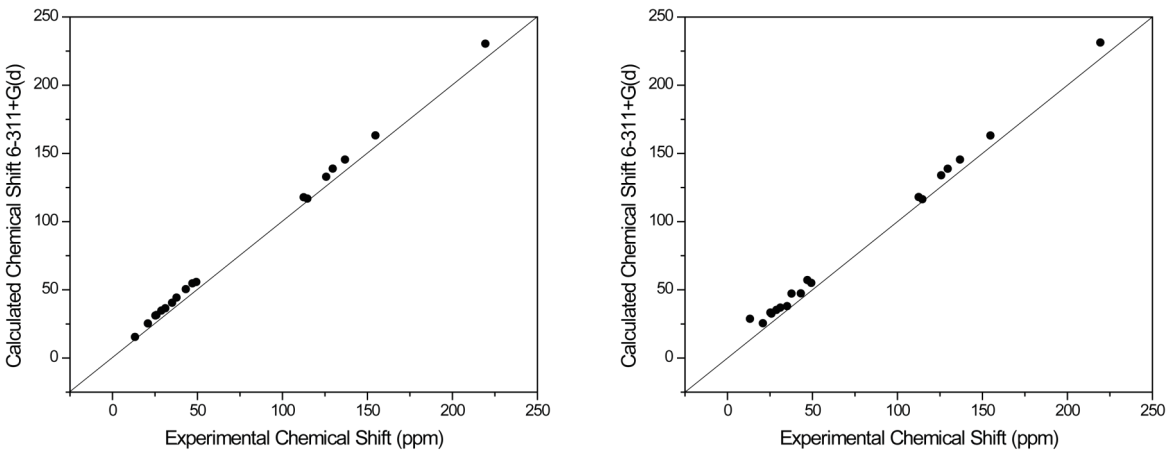

Figure S5. Correlation between the experimental isotropic ^{13}C chemical shifts for estrone *versus* calculated isotropic ^{13}C chemical shifts for estrone (a) and 13-*epi*-estrone (b) (experiment in DMSO, calculation in vacuum).

MSpin output

1) Order parameters from the SVD fitting to the structure of estrone using the ΔΔRCSAs and ΔRDCs data.

estrone

Distribution size=512
Distribution type=Gaussian
Alignment tensor
<Axx>=0.000107772 stdved=6.39355e-05
<Ayy>=0.000280701 stdved=0.000138212
<Azz>=-0.000388473 stdved=0.000172194
Quality factors statistic
<Q>=0.32771
StdDev(Q)=0.0632431
Highest Q=0.613112
Lowest Q=0.22753

2) Order parameters from the SVD fitting to the structure of 13-*epi*-estrone using the ΔΔRCSAs and ΔRDCs data.

13-*epi*-estrone

Distribution size=512
Distribution type=Gaussian
Alignment tensor
<Axx>=0.000105375 stdved=3.27003e-05
<Ayy>=0.000373731 stdved=0.000154304
<Azz>=-0.000479106 stdved=0.000167089
Quality factors statistic
<Q>=0.452561
StdDev(Q)=0.0485404
Highest Q=0.689082
Lowest Q=0.383281

3) Order parameters from the SVD fitting to the structure of estrone using only the ΔΔRCSAs data.

estrone

Distribution size=512
Distribution type=Gaussian
Alignment tensor
<Axx>=6.56785e-05 stdved=0.000122571
<Ayy>=0.000328564 stdved=0.000855862
<Azz>=-0.000394243 stdved=0.000941495
Quality factors statistic
<Q>=0.352168

StdDev(Q)=0.0566843
Highest Q=0.647872
Lowest Q=0.254074

4) Order parameters from the SVD fitting to the structure of 13-*epi*-estrone using only the ΔΔRCSAs.

<u>13-*epi*-estrone</u>

Distribution size=512
Distribution type=Gaussian
Alignment tensor
<Axx>=0.000191934 stdved=9.66323e-05
<Ayy>=0.000870676 stdved=0.000374817
<Azz>=-0.00106261 stdved=0.000386047
Quality factors statistic
<Q>=0.33947
StdDev(Q)=0.0561429
Highest Q=0.598498
Lowest Q=0.241752

Gaussian03 output

B3LYP computed geometries (XYZ, angstroms), energies (hartrees)

estrone (Conformation 2 – Table S3)
nmr=(giao,spinspin) rb3lyp/6-311+g(d) geom=connectivity

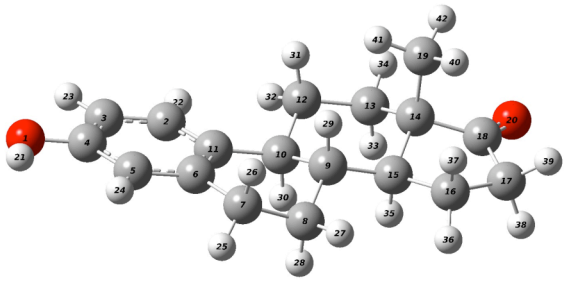

Figure S6. 3D structure of estrone: geometry optimized (in vacuum) using DFT (functional: B3LYP, basis set 6-311+G(d)), numbering from Gaussian.

O	5.953281	-0.239772	0.277784
C	2.598669	-1.517281	-0.345181
C	3.978049	-1.473760	-0.163275
C	4.590418	-0.247581	0.105461
C	3.812138	0.906177	0.182232
C	2.421551	0.860798	-0.000328
C	1.641750	2.160248	0.117508
C	0.217834	2.069726	-0.439595
C	-0.463397	0.790011	0.058635
C	0.278690	-0.446139	-0.521547
C	1.787624	-0.370517	-0.264498
C	-0.374336	-1.775645	-0.066942
C	-1.895839	-1.833103	-0.331849
C	-2.601848	-0.604205	0.252365
C	-1.943840	0.681439	-0.313375
C	-2.945379	1.805634	0.026682
C	-4.313986	1.133014	-0.240527
C	-4.060775	-0.383832	-0.159475
C	-2.630834	-0.671621	1.804738
O	-4.886858	-1.245169	-0.387127
H	6.255814	0.664296	0.455970
H	2.148056	-2.480960	-0.560619
H	4.584369	-2.372168	-0.229472
H	4.288866	1.865857	0.385473
H	2.195209	2.967138	-0.380637
H	1.589438	2.444147	1.180300
H	-0.349144	2.959243	-0.137542
H	0.240354	2.065948	-1.539764
H	-0.368192	0.772006	1.155955
H	0.135361	-0.391093	-1.615955
H	-0.165960	-1.934538	0.999707

```
H                      0.088378   -2.618064   -0.592682
H                     -2.076344   -1.868040   -1.415489
H                     -2.314637   -2.758712    0.081359
H                     -1.978650    0.574198   -1.413054
H                     -2.798179    2.698804   -0.588863
H                     -2.852973    2.117199    1.074521
H                     -4.689638    1.355577   -1.247649
H                     -5.108085    1.421666    0.457657
H                     -3.126152    0.195496    2.255147
H                     -1.625004   -0.732578    2.229770
H                     -3.183189   -1.566071    2.114435
```

Calculating GIAO nuclear magnetic shielding tensors.
SCF GIAO Magnetic shielding tensor (ppm):
1 O Isotropic = 205.1911 Anisotropy = 74.9041
XX= 252.5247 YX= 6.8653 ZX= 7.4078
XY= 21.0271 YY= 161.8679 ZY= -3.8424
XZ= 5.1624 YZ= -9.9252 ZZ= 201.1808
Eigenvalues: 158.3620 202.0842 255.1272
2 C Isotropic = 50.5585 Anisotropy = 177.2031
XX= 27.6835 YX= -29.1260 ZX= -23.5710
XY= -32.8083 YY= -34.6391 ZY= -34.9305
XZ= -32.7752 YZ= -36.4835 ZZ= 158.6310
Eigenvalues: -56.3787 39.3602 168.6939
3 C Isotropic = 65.5429 Anisotropy = 145.3530
XX= 34.8218 YX= 40.7405 ZX= -10.1136
XY= 33.7324 YY= 4.4828 ZY= -20.7824
XZ= -13.1109 YZ= -21.3426 ZZ= 157.3242
Eigenvalues: -21.2550 55.4389 162.4450
4 C Isotropic = 20.2411 Anisotropy = 139.2140
XX= -64.0722 YX= -7.1747 ZX= -23.4669
XY= -1.5259 YY= 16.9877 ZY= -15.1022
XZ= -19.4083 YZ= -17.8304 ZZ= 107.8079
Eigenvalues: -67.1891 14.8621 113.0504
5 C Isotropic = 66.5529 Anisotropy = 108.5388
XX= 56.4295 YX= -38.0114 ZX= -15.4879
XY= -28.4501 YY= 10.2091 ZY= -23.7544
XZ= -8.0210 YZ= -29.8199 ZZ= 133.0201
Eigenvalues: -12.9927 73.7392 138.9121
6 C Isotropic = 37.9798 Anisotropy = 185.7967
XX= -7.5581 YX= 32.7377 ZX= -15.7743
XY= 31.5156 YY= -34.9673 ZY= -24.9782
XZ= -20.2061 YZ= -19.6408 ZZ= 156.4648
Eigenvalues: -56.5641 8.6593 161.8443
7 C Isotropic = 148.6471 Anisotropy = 23.0707
XX= 160.8579 YX= -1.2405 ZX= 5.1541
XY= -12.3386 YY= 148.9418 ZY= -2.6198
XZ= -1.2907 YZ= 3.2814 ZZ= 136.1417
Eigenvalues: 135.9263 145.9875 164.0276
8 C Isotropic = 151.8770 Anisotropy = 16.9362
XX= 150.3269 YX= 10.3385 ZX= -0.1023

```
  XY=    9.3129   YY=   154.5292   ZY=    -3.8056
  XZ=   -2.7190   YZ=    -1.4403   ZZ=   150.7750
  Eigenvalues:   142.3420   150.1212   163.1678
 9  C    Isotropic =   139.0999   Anisotropy =     6.4382
  XX=   140.0425   YX=    -6.3656   ZX=     0.3919
  XY=    2.2237   YY=   136.8856   ZY=    -1.2605
  XZ=    5.2860   YZ=     1.1875   ZZ=   140.3717
  Eigenvalues:   135.4581   138.4496   143.3921
10  C    Isotropic =   132.9437   Anisotropy =     9.5829
  XX=   129.3235   YX=   -11.1439   ZX=    -5.6069
  XY=   -5.2146   YY=   130.4515   ZY=    -1.1526
  XZ=    2.5931   YZ=    -1.9687   ZZ=   139.0561
  Eigenvalues:   121.4226   138.0761   139.3323
11  C    Isotropic =    44.5702   Anisotropy =   176.4921
  XX=   -39.6211   YX=     0.7233   ZX=   -26.8260
  XY=    0.2936   YY=    19.1702   ZY=   -21.8933
  XZ=   -23.8644   YZ=   -30.8647   ZZ=   154.1616
  Eigenvalues:   -43.0205    14.4995   162.2316
12  C    Isotropic =   152.2987   Anisotropy =    19.3763
  XX=   157.7568   YX=     8.1646   ZX=    -0.5140
  XY=    6.2905   YY=   155.2285   ZY=    -7.9978
  XZ=    1.5298   YZ=    -8.9225   ZZ=   143.9108
  Eigenvalues:   138.5400   153.1398   165.2162
13  C    Isotropic =   146.9521   Anisotropy =    18.8246
  XX=   144.4239   YX=    -7.7612   ZX=    -8.3432
  XY=   -2.2697   YY=   150.6490   ZY=     9.9664
  XZ=   -5.1963   YZ=     3.0482   ZZ=   145.7833
  Eigenvalues:   138.2441   143.1103   159.5018
14  C    Isotropic =   128.6597   Anisotropy =    21.1371
  XX=   139.6825   YX=   -14.1438   ZX=    -5.8552
  XY=   -2.5363   YY=   120.0297   ZY=    -0.2031
  XZ=    5.2307   YZ=    -3.3943   ZZ=   126.2670
  Eigenvalues:   116.6326   126.5955   142.7512
15  C    Isotropic =   127.6611   Anisotropy =    20.0263
  XX=   140.9191   YX=     6.5784   ZX=     4.8407
  XY=   -4.5243   YY=   128.2324   ZY=     3.7794
  XZ=   -6.5023   YZ=     4.0533   ZZ=   113.8316
  Eigenvalues:   112.7956   129.1757   141.0119
16  C    Isotropic =   158.1135   Anisotropy =    23.0500
  XX=   171.0088   YX=    -8.9601   ZX=     1.0229
  XY=   -4.0357   YY=   156.0898   ZY=     4.3985
  XZ=    3.7117   YZ=     2.6330   ZZ=   147.2419
  Eigenvalues:   145.1982   155.6621   173.4802
17  C    Isotropic =   142.9307   Anisotropy =    34.5509
  XX=   141.1743   YX=    -0.0321   ZX=     7.9062
  XY=    1.1067   YY=   165.8860   ZY=     1.3530
  XZ=    0.2241   YZ=     1.8865   ZZ=   121.7317
  Eigenvalues:   120.8671   141.9603   165.9646
18  C    Isotropic =   -46.9553   Anisotropy =   164.9838
  XX=   -77.6330   YX=    21.0722   ZX=   -39.5626
  XY=    15.5017   YY=  -116.5008   ZY=     1.4832
```

```
  XZ=   -34.4965   YZ=     4.5580   ZZ=    53.2680
  Eigenvalues:  -125.4597   -78.4400    63.0340
 19  C    Isotropic =   168.0216   Anisotropy =    24.4809
  XX=   157.3162   YX=     7.4082   ZX=    -3.8789
  XY=     8.1620   YY=   164.1671   ZY=    -6.1306
  XZ=    -3.3035   YZ=    -1.3962   ZZ=   182.5813
  Eigenvalues:   152.2050   167.5175   184.3422
 20  O    Isotropic =  -289.0490   Anisotropy =   970.8563
  XX=  -547.6379   YX=  -207.4533   ZX=  -254.4812
  XY=  -205.6957   YY=  -602.6167   ZY=   -63.8286
  XZ=  -266.4471   YZ=   -81.0541   ZZ=   283.1077
  Eigenvalues:  -831.4214  -393.9141   358.1886
 21  H    Isotropic =    28.5202   Anisotropy =    11.3940
  XX=    31.7411   YX=     4.2408   ZX=     1.9215
  XY=     2.6329   YY=    32.3997   ZY=     2.0975
  XZ=     1.8459   YZ=     2.4574   ZZ=    21.4198
  Eigenvalues:    20.8244    28.6200    36.1162
 22  H    Isotropic =    24.9541   Anisotropy =    10.7736
  XX=    31.0330   YX=    -3.2257   ZX=    -0.3406
  XY=    -2.6672   YY=    24.1281   ZY=     0.5951
  XZ=    -0.2701   YZ=     0.4164   ZZ=    19.7012
  Eigenvalues:    19.6441    23.0816    32.1365
 23  H    Isotropic =    25.3849   Anisotropy =     4.7558
  XX=    28.0607   YX=     1.3989   ZX=     0.8431
  XY=     0.4048   YY=    26.0866   ZY=     0.6525
  XZ=     0.6628   YZ=     0.8237   ZZ=    22.0073
  Eigenvalues:    21.8207    25.7785    28.5554
 24  H    Isotropic =    25.9574   Anisotropy =     8.1838
  XX=    30.7208   YX=    -1.9818   ZX=     0.7447
  XY=    -2.0638   YY=    25.2352   ZY=     0.2019
  XZ=     0.4011   YZ=     0.0282   ZZ=    21.9164
  Eigenvalues:    21.8586    24.6005    31.4133
 25  H    Isotropic =    29.3573   Anisotropy =     9.1434
  XX=    32.5782   YX=     2.8788   ZX=    -0.3929
  XY=     3.2940   YY=    31.4411   ZY=    -1.7553
  XZ=    -0.1691   YZ=    -3.2763   ZZ=    24.0524
  Eigenvalues:    23.2279    29.3910    35.4529
 26  H    Isotropic =    29.1746   Anisotropy =     7.2774
  XX=    30.0264   YX=    -0.2736   ZX=     2.0441
  XY=     0.7544   YY=    28.2024   ZY=     3.9013
  XZ=     0.9200   YZ=     5.7785   ZZ=    29.2952
  Eigenvalues:    23.7709    29.7267    34.0263
 27  H    Isotropic =    30.2062   Anisotropy =     7.1688
  XX=    32.4914   YX=    -0.8559   ZX=    -0.1887
  XY=    -1.3245   YY=    34.4146   ZY=     0.9091
  XZ=    -0.3161   YZ=     0.9284   ZZ=    23.7124
  Eigenvalues:    23.6312    32.0019    34.9854
 28  H    Isotropic =    30.7554   Anisotropy =     6.1961
  XX=    29.9618   YX=     1.6455   ZX=     0.2445
  XY=     1.2003   YY=    29.5326   ZY=    -3.0249
  XZ=     0.7933   YZ=    -3.6561   ZZ=    32.7718
```

```
  Eigenvalues:    26.7532    30.6268    34.8861
29  H    Isotropic =    30.4565   Anisotropy =     4.5488
  XX=    31.5055   YX=     2.5492   ZX=    -0.3282
  XY=     2.7441   YY=    28.8653   ZY=    -0.0940
  XZ=    -1.9417   YZ=     0.2865   ZZ=    30.9989
  Eigenvalues:    27.1050    30.7756    33.4891
30  H    Isotropic =    29.8296   Anisotropy =     2.2307
  XX=    29.8442   YX=     0.6149   ZX=    -1.7003
  XY=    -0.4544   YY=    28.4642   ZY=     0.5714
  XZ=     1.1836   YZ=     0.4749   ZZ=    31.1804
  Eigenvalues:    28.3560    29.8160    31.3167
31  H    Isotropic =    30.6149   Anisotropy =     5.1595
  XX=    31.5008   YX=    -0.9691   ZX=     1.2589
  XY=    -1.6626   YY=    29.6305   ZY=    -3.4269
  XZ=    -1.1118   YZ=    -3.5707   ZZ=    30.7133
  Eigenvalues:    26.4482    31.3419    34.0545
32  H    Isotropic =    29.8293   Anisotropy =    10.0257
  XX=    32.3386   YX=    -2.3066   ZX=    -1.3834
  XY=    -2.9127   YY=    33.6365   ZY=     2.9787
  XZ=    -1.5289   YZ=     3.0888   ZZ=    23.5128
  Eigenvalues:    22.6178    30.3571    36.5131
33  H    Isotropic =    30.6838   Anisotropy =     7.5886
  XX=    29.7942   YX=     0.3957   ZX=     1.7383
  XY=     0.4618   YY=    29.7447   ZY=     3.9719
  XZ=     1.5145   YZ=     3.9479   ZZ=    32.5126
  Eigenvalues:    26.8041    29.5045    35.7429
34  H    Isotropic =    30.1697   Anisotropy =     9.1116
  XX=    30.2434   YX=     2.4271   ZX=    -0.7875
  XY=     3.3041   YY=    34.7987   ZY=    -0.4178
  XZ=    -1.1066   YZ=    -0.4868   ZZ=    25.4670
  Eigenvalues:    25.2849    28.9800    36.2441
35  H    Isotropic =    30.5468   Anisotropy =     2.3355
  XX=    30.2970   YX=    -1.2304   ZX=     1.2184
  XY=    -1.9584   YY=    29.4620   ZY=     0.0589
  XZ=    -0.9077   YZ=    -0.8010   ZZ=    31.8813
  Eigenvalues:    28.2205    31.3160    32.1038
36  H    Isotropic =    30.1919   Anisotropy =     8.1307
  XX=    30.3635   YX=    -0.8667   ZX=     0.2324
  XY=    -0.1251   YY=    33.8973   ZY=    -3.5366
  XZ=     0.3704   YZ=    -4.2759   ZZ=    26.3149
  Eigenvalues:    24.6613    30.3019    35.6124
37  H    Isotropic =    30.5960   Anisotropy =     6.7131
  XX=    29.6080   YX=    -1.1696   ZX=    -0.8707
  XY=    -0.7588   YY=    30.4860   ZY=     3.5242
  XZ=    -0.4140   YZ=     3.8856   ZZ=    31.6939
  Eigenvalues:    27.2891    29.4274    35.0714
38  H    Isotropic =    30.0170   Anisotropy =     8.7211
  XX=    31.7342   YX=     0.5057   ZX=     4.3696
  XY=    -0.7189   YY=    28.0038   ZY=    -1.8169
  XZ=     4.7076   YZ=    -1.8636   ZZ=    30.3129
  Eigenvalues:    25.6305    28.5894    35.8311
```

39 H Isotropic = 29.7624 Anisotropy = 8.4871
XX= 34.2435 YX= -1.2490 ZX= -2.0409
XY= -1.8940 YY= 27.5537 ZY= 1.3019
XZ= -2.4862 YZ= 1.7386 ZZ= 27.4901
Eigenvalues: 25.9560 27.9108 35.4205
40 H Isotropic = 31.3087 Anisotropy = 8.3234
XX= 28.5420 YX= -2.1280 ZX= -3.9419
XY= -2.4146 YY= 31.1584 ZY= 0.3363
XZ= -3.3901 YZ= 2.2037 ZZ= 34.2256
Eigenvalues: 26.2514 30.8170 36.8576
41 H Isotropic = 31.0256 Anisotropy = 5.0195
XX= 32.7735 YX= 0.0602 ZX= 0.9188
XY= -0.0174 YY= 27.0102 ZY= -1.1008
XZ= 1.4925 YZ= -1.1651 ZZ= 33.2931
Eigenvalues: 26.8031 31.9018 34.3719
42 H Isotropic = 31.5808 Anisotropy = 10.5800
XX= 30.0785 YX= 3.8046 ZX= -3.0435
XY= 3.2765 YY= 32.6922 ZY= -3.1602
XZ= -3.2548 YZ= -4.1605 ZZ= 31.9716
Eigenvalues: 27.4531 28.6551 38.6341

13-epi-estrone (Conformation 4 – Table S3)

nmr=(giao,spinspin) rb3lyp/6-311+g(d) geom=connectivity

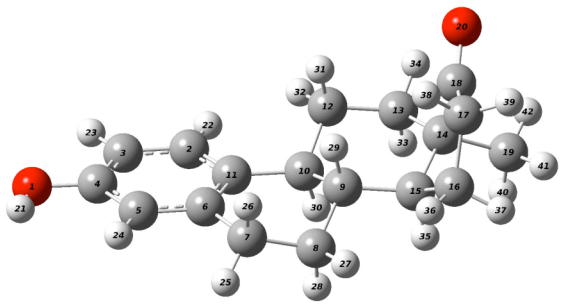

Figure S7. 3D structure of 13-epi-estrone: geometry optimized (in vacuum) using DFT (functional: B3LYP, basis set 6-311+G(d)), numbering from Gaussian.

O	5.832763	-0.255921	0.524295
C	2.515252	-1.545315	-0.250587
C	3.881131	-1.499191	0.010443
C	4.483259	-0.264728	0.267425
C	3.710307	0.894592	0.243660
C	2.332883	0.845148	-0.021793
C	1.552157	2.146906	-0.042964
C	0.205682	2.015249	-0.759230
C	-0.557646	0.792448	-0.230461
C	0.214485	-0.494501	-0.594919
C	1.707144	-0.393419	-0.261938

C	-0.498178	-1.699816	0.046480
C	-1.916792	-1.845400	-0.511991
C	-2.770135	-0.572292	-0.396877
C	-2.030248	0.761206	-0.717221
C	-2.891566	1.836731	0.010458
C	-3.370178	1.160090	1.309215
C	-3.301887	-0.341692	1.031142
C	-4.028863	-0.731448	-1.291235
O	-3.631797	-1.215143	1.809066
H	6.129061	0.652905	0.688095
H	2.071602	-2.514956	-0.456817
H	4.485760	-2.401164	0.015532
H	4.180685	1.861233	0.427356
H	2.159337	2.931663	-0.513018
H	1.375893	2.480116	0.991891
H	-0.370959	2.938099	-0.625421
H	0.365729	1.897896	-1.841594
H	-0.563253	0.858673	0.871581
H	0.133319	-0.620098	-1.690233
H	-0.522148	-1.571980	1.138123
H	0.043950	-2.632053	-0.142829
H	-1.848582	-2.124498	-1.573880
H	-2.444461	-2.660926	-0.002540
H	-2.029900	0.935781	-1.802699
H	-2.331670	2.756526	0.204039
H	-3.748574	2.118912	-0.611463
H	-2.709772	1.372796	2.160128
H	-4.380576	1.443369	1.624839
H	-3.728216	-0.796336	-2.344111
H	-4.730369	0.104823	-1.193902
H	-4.565424	-1.649682	-1.027585

Calculating GIAO nuclear magnetic shielding tensors.
SCF GIAO Magnetic shielding tensor (ppm):

1 O Isotropic = 205.1346 Anisotropy = 73.9553
XX= 251.0661 YX= 6.4647 ZX= 10.2638
XY= 20.7142 YY= 160.9256 ZY= -1.4958
XZ= 7.6330 YZ= -5.6051 ZZ= 203.4121
Eigenvalues: 158.3972 202.5684 254.4381
2 C Isotropic = 49.4626 Anisotropy = 178.3862
XX= 28.7830 YX= -28.3936 ZX= -29.9614
XY= -35.5495 YY= -37.6462 ZY= -29.7362
XZ= -39.9760 YZ= -29.7435 ZZ= 157.2509
Eigenvalues: -58.3648 38.3658 168.3867
3 C Isotropic = 65.3947 Anisotropy = 145.4427
XX= 37.1835 YX= 40.9800 ZX= -19.0253
XY= 33.7554 YY= 2.4944 ZY= -12.8600
XZ= -21.7369 YZ= -13.7779 ZZ= 156.5062
Eigenvalues: -21.3583 55.1859 162.3564
4 C Isotropic = 20.3362 Anisotropy = 138.9026
XX= -60.1882 YX= -7.3912 ZX= -33.8799

```
 XY=   -1.2891   YY=   15.2832   ZY=  -11.2766
 XZ=  -28.5955   YZ=  -13.5611   ZZ=  105.9136
 Eigenvalues:  -66.3894   14.4600  112.9379
5  C   Isotropic =   67.0052   Anisotropy =  107.5921
 XX=   57.8937   YX=  -37.3319   ZX=  -17.9881
 XY=  -28.4953   YY=    9.1659   ZY=  -19.7456
 XZ=  -10.8436   YZ=  -24.0131   ZZ=  133.9560
 Eigenvalues:  -12.0625   74.3448  138.7332
6  C   Isotropic =   37.9183   Anisotropy =  185.3113
 XX=   -5.3130   YX=   32.2740   ZX=  -27.6365
 XY=   29.9885   YY=  -35.7862   ZY=  -11.7044
 XZ=  -32.5050   YZ=   -7.1664   ZZ=  154.8541
 Eigenvalues:  -55.5273    7.8230  161.4591
7  C   Isotropic =  148.1935   Anisotropy =   21.5707
 XX=  159.3273   YX=   -0.6788   ZX=    7.5919
 XY=  -10.8648   YY=  147.5715   ZY=   -4.7176
 XZ=    0.8855   YZ=    0.6276   ZZ=  137.6816
 Eigenvalues:  136.7856  145.2209  162.5739
8  C   Isotropic =  150.8574   Anisotropy =   18.7410
 XX=  152.0579   YX=   10.4189   ZX=    1.3468
 XY=   12.4110   YY=  150.4000   ZY=   -5.8618
 XZ=   -1.6395   YZ=   -2.4930   ZZ=  150.1142
 Eigenvalues:  138.9712  150.2496  163.3513
9  C   Isotropic =  136.1817   Anisotropy =    9.0964
 XX=  130.9209   YX=   -6.0626   ZX=   -0.8853
 XY=    6.5788   YY=  137.1938   ZY=    2.6714
 XZ=    4.4831   YZ=    2.8036   ZZ=  140.4303
 Eigenvalues:  130.5823  135.7168  142.2459
10  C   Isotropic =  136.0326   Anisotropy =   12.0843
 XX=  133.2366   YX=   -7.7424   ZX=   -1.4015
 XY=    6.3735   YY=  131.9699   ZY=   -2.5720
 XZ=    7.2074   YZ=   -1.5709   ZZ=  142.8913
 Eigenvalues:  131.5656  132.4434  144.0888
11  C   Isotropic =   44.6569   Anisotropy =  175.9635
 XX=  -36.0839   YX=    1.9401   ZX=  -37.0702
 XY=    0.5885   YY=   18.1765   ZY=  -15.6477
 XZ=  -35.1106   YZ=  -28.8283   ZZ=  151.8781
 Eigenvalues:  -42.9100   14.9149  161.9660
12  C   Isotropic =  150.0903   Anisotropy =   14.1357
 XX=  152.7310   YX=    6.9267   ZX=   -0.8334
 XY=    4.7587   YY=  152.1454   ZY=   -6.3129
 XZ=   -2.0972   YZ=   -2.5194   ZZ=  145.3944
 Eigenvalues:  142.9691  147.7877  159.5141
13  C   Isotropic =  146.5152   Anisotropy =   28.2915
 XX=  158.6741   YX=   -6.2284   ZX=    7.9333
 XY=  -15.2268   YY=  141.9014   ZY=   -0.0197
 XZ=    7.5835   YZ=    3.8956   ZZ=  138.9700
 Eigenvalues:  132.0592  142.1102  165.3762
14  C   Isotropic =  126.2640   Anisotropy =   26.3106
 XX=  131.1737   YX=   -5.4720   ZX=   -8.7473
 XY=   -1.4962   YY=  116.0074   ZY=    2.7899
```

XZ= -9.7951 YZ= 16.1452 ZZ= 131.6109
Eigenvalues: 111.5001 123.4876 143.8044
15 C Isotropic = 128.4220 Anisotropy = 18.6924
XX= 127.8061 YX= 11.4570 ZX= -10.0447
XY= 11.9375 YY= 129.4316 ZY= 1.4954
XZ= -0.4169 YZ= 1.3357 ZZ= 128.0282
Eigenvalues: 115.0850 129.2973 140.8836
16 C Isotropic = 157.9580 Anisotropy = 26.8297
XX= 154.7406 YX= -9.2247 ZX= -8.7680
XY= -4.6918 YY= 156.2606 ZY= 4.2332
XZ= -14.1689 YZ= 9.7931 ZZ= 162.8729
Eigenvalues: 146.2081 151.8215 175.8445
17 C Isotropic = 145.4116 Anisotropy = 39.7326
XX= 127.7894 YX= -3.1788 ZX= -8.6119
XY= -6.6747 YY= 171.3492 ZY= 1.9100
XZ= -1.4068 YZ= -2.7428 ZZ= 137.0962
Eigenvalues: 125.1293 139.2054 171.9000
18 C Isotropic = -47.8227 Anisotropy = 168.6459
XX= 42.4729 YX= 5.1832 ZX= 55.9552
XY= 2.2992 YY= -116.0434 ZY= -12.9104
XZ= 53.0675 YZ= -19.2510 ZZ= -69.8975
Eigenvalues: -124.3091 -83.7669 64.6079
19 C Isotropic = 154.7066 Anisotropy = 44.8086
XX= 168.2818 YX= 9.0774 ZX= 17.5779
XY= 10.7707 YY= 137.0305 ZY= -2.0628
XZ= 21.3529 YZ= -1.1824 ZZ= 158.8076
Eigenvalues: 131.5528 147.9880 184.5790
20 O Isotropic = -296.3296 Anisotropy = 993.9440
XX= 237.7840 YX= -66.8375 ZX= 318.4181
XY= -92.4063 YY= -629.8376 ZY= 198.1903
XZ= 347.7324 YZ= 216.8406 ZZ= -496.9353
Eigenvalues: -849.9210 -405.3676 366.2997
21 H Isotropic = 28.5577 Anisotropy = 11.4554
XX= 31.5718 YX= 4.1880 ZX= 2.4375
XY= 2.6357 YY= 32.5493 ZY= 1.8280
XZ= 2.5240 YZ= 2.2576 ZZ= 21.5521
Eigenvalues: 20.8310 28.6475 36.1947
22 H Isotropic = 24.9499 Anisotropy = 10.5923
XX= 30.7865 YX= -3.3813 ZX= 0.1534
XY= -2.7310 YY= 24.2905 ZY= 0.0385
XZ= 0.6216 YZ= -0.2586 ZZ= 19.7727
Eigenvalues: 19.7591 23.0792 32.0115
23 H Isotropic = 25.3559 Anisotropy = 4.7813
XX= 27.9388 YX= 1.3714 ZX= 1.1682
XY= 0.4138 YY= 26.1359 ZY= 0.5187
XZ= 0.9746 YZ= 0.8206 ZZ= 21.9929
Eigenvalues: 21.7452 25.7790 28.5434
24 H Isotropic = 26.0159 Anisotropy = 8.1514
XX= 30.6842 YX= -1.8365 ZX= 1.3287
XY= -2.0499 YY= 25.2706 ZY= -0.0005
XZ= 1.0066 YZ= -0.2298 ZZ= 22.0928

```
  Eigenvalues:    21.9299    24.6675    31.4501
25  H    Isotropic =    29.4111   Anisotropy =     9.2828
  XX=    32.7642   YX=     3.1351   ZX=     0.1695
  XY=     3.4090   YY=    31.3993   ZY=    -1.7931
  XZ=     0.3622   YZ=    -3.2401   ZZ=    24.0698
  Eigenvalues:    23.1153    29.5183    35.5996
26  H    Isotropic =    29.2531   Anisotropy =     6.8886
  XX=    29.9452   YX=    -0.4051   ZX=     1.8865
  XY=     0.4051   YY=    28.6925   ZY=     3.7761
  XZ=     0.7381   YZ=     5.6190   ZZ=    29.1217
  Eigenvalues:    24.0626    29.8511    33.8455
27  H    Isotropic =    30.1701   Anisotropy =     6.4600
  XX=    32.4040   YX=    -0.5157   ZX=    -0.0953
  XY=    -1.3449   YY=    34.0588   ZY=    -0.2612
  XZ=     0.0375   YZ=     0.1128   ZZ=    24.0474
  Eigenvalues:    24.0467    31.9868    34.4767
28  H    Isotropic =    30.6671   Anisotropy =     6.3583
  XX=    29.7301   YX=     2.2514   ZX=    -0.6135
  XY=     1.2315   YY=    28.8918   ZY=    -2.6992
  XZ=     0.0461   YZ=    -2.8378   ZZ=    33.3795
  Eigenvalues:    26.8171    30.2783    34.9060
29  H    Isotropic =    31.1135   Anisotropy =     3.5404
  XX=    33.2935   YX=     1.0988   ZX=    -0.1641
  XY=     0.3178   YY=    28.6557   ZY=     1.1011
  XZ=    -0.9383   YZ=     1.4320   ZZ=    31.3912
  Eigenvalues:    28.0185    31.8481    33.4737
30  H    Isotropic =    29.7908   Anisotropy =     2.3296
  XX=    30.7564   YX=     0.5086   ZX=    -1.4681
  XY=    -0.7219   YY=    28.0673   ZY=     1.3877
  XZ=     1.5693   YZ=     1.8404   ZZ=    30.5488
  Eigenvalues:    27.2683    30.7603    31.3439
31  H    Isotropic =    31.1301   Anisotropy =     4.8686
  XX=    31.3091   YX=    -0.2946   ZX=     1.1713
  XY=    -0.1824   YY=    29.3362   ZY=    -2.6870
  XZ=    -0.6407   YZ=    -2.9546   ZZ=    32.7449
  Eigenvalues:    27.7431    31.2712    34.3758
32  H    Isotropic =    30.0128   Anisotropy =    10.2266
  XX=    33.2032   YX=    -2.9210   ZX=     0.2566
  XY=    -3.3557   YY=    34.1152   ZY=     0.2442
  XZ=    -0.1842   YZ=    -0.1733   ZZ=    22.7199
  Eigenvalues:    22.7196    30.4883    36.8305
33  H    Isotropic =    30.7148   Anisotropy =     6.4267
  XX=    30.7791   YX=    -1.0521   ZX=     1.8760
  XY=    -0.5712   YY=    30.4826   ZY=     4.2633
  XZ=     1.1607   YZ=     4.2122   ZZ=    30.8828
  Eigenvalues:    25.8897    31.2555    34.9993
34  H    Isotropic =    29.6173   Anisotropy =     7.7147
  XX=    30.3787   YX=     2.3553   ZX=    -0.8714
  XY=     2.5790   YY=    32.7003   ZY=    -2.2940
  XZ=    -0.7681   YZ=    -1.6524   ZZ=    25.7728
  Eigenvalues:    25.2441    28.8472    34.7604
```

35 H Isotropic = 30.3803 Anisotropy = 3.3170
XX= 30.6815 YX= 1.1585 ZX= 0.7567
XY= 0.4257 YY= 28.3505 ZY= -0.7613
XZ= 1.0402 YZ= -0.9548 ZZ= 32.1089
Eigenvalues: 27.8246 30.7247 32.5917
36 H Isotropic = 30.2488 Anisotropy = 6.7091
XX= 30.4795 YX= 1.3735 ZX= -1.7626
XY= 1.5437 YY= 34.1481 ZY= 0.8600
XZ= -1.4192 YZ= 1.7505 ZZ= 26.1187
Eigenvalues: 25.2709 30.7540 34.7215
37 H Isotropic = 30.1057 Anisotropy = 9.4344
XX= 32.2873 YX= -4.6009 ZX= 3.2119
XY= -3.8168 YY= 29.4134 ZY= -1.3228
XZ= 2.2539 YZ= -1.0555 ZZ= 28.6162
Eigenvalues: 26.1507 27.7710 36.3953
38 H Isotropic = 29.9506 Anisotropy = 6.9731
XX= 28.2213 YX= 1.3425 ZX= 0.5584
XY= 0.8423 YY= 27.2581 ZY= 1.4068
XZ= -0.0771 YZ= 1.0082 ZZ= 34.3723
Eigenvalues: 26.4444 28.8080 34.5993
39 H Isotropic = 29.8624 Anisotropy = 8.7602
XX= 32.5255 YX= -1.8519 ZX= -4.2107
XY= -2.5081 YY= 27.7591 ZY= 0.9338
XZ= -3.7187 YZ= -0.2549 ZZ= 29.3027
Eigenvalues: 25.9827 27.9020 35.7025
40 H Isotropic = 31.2547 Anisotropy = 8.2325
XX= 29.9603 YX= 0.8124 ZX= 3.1747
XY= 0.6332 YY= 28.2142 ZY= 1.1908
XZ= 1.7582 YZ= 1.2280 ZZ= 35.5896
Eigenvalues: 27.9331 29.0880 36.7430
41 H Isotropic = 30.9174 Anisotropy = 8.8596
XX= 35.4664 YX= -2.8027 ZX= 3.5440
XY= -0.9678 YY= 30.1881 ZY= 1.7680
XZ= 2.6706 YZ= 0.3838 ZZ= 27.0978
Eigenvalues: 25.4923 30.4362 36.8238
42 H Isotropic = 31.1930 Anisotropy = 9.7781
XX= 33.8949 YX= 5.4738 ZX= 1.4356
XY= 3.6167 YY= 32.0263 ZY= -0.2530
XZ= 1.5938 YZ= -0.1433 ZZ= 27.6578
Eigenvalues: 26.7637 29.1036 37.7117

TMS
nmr=giao rb3lyp/6-311+g(d) geom=connectivity

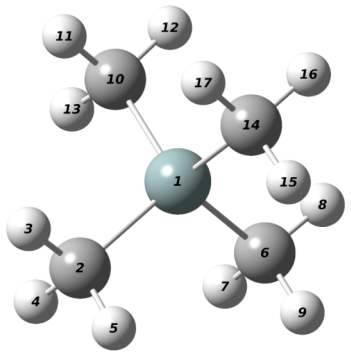

Figure S8. 3D structure of TMS: geometry optimized (in vacuum) using DFT (functional: B3LYP, basis set 6-311+G(d)), numbering from Gaussian.

Si	-0.00032	-0.00032	-0.00032
C	-1.39174	-1.25061	0.312
H	-2.16956	-0.82988	0.9625
H	-1.87503	-1.55462	-0.62565
H	-1.01224	-2.15937	0.79705
C	1.31502	-0.78299	-1.12014
H	0.89225	-1.08001	-2.08872
H	2.13793	-0.08431	-1.31998
H	1.74907	-1.68052	-0.66056
C	-0.71348	1.54159	-0.84324
H	-1.47868	2.02092	-0.21885
H	0.06715	2.28817	-1.03924
H	-1.18097	1.29326	-1.80503
C	0.79042	0.49228	1.65163
H	1.21464	-0.37851	2.16839
H	1.60224	1.2168	1.50613
H	0.05632	0.95094	2.32689

Calculating GIAO nuclear magnetic shielding tensors.
SCF GIAO Magnetic shielding tensor (ppm):

1 Si Isotropic = 337.8031 Anisotropy = 0.3690
XX= 337.6873 YX= 0.2432 ZX= -0.1812
XY= 0.0328 YY= 337.9782 ZY= 0.0707
XZ= -0.0053 YZ= 0.1442 ZZ= 337.7439
Eigenvalues: 337.5472 337.8130 338.0492
2 C Isotropic = 183.2479 Anisotropy = 9.6250
XX= 185.2392 YX= 4.6373 ZX= -1.1313
XY= 4.6875 YY= 184.2154 ZY= -1.0277
XZ= -1.1392 YZ= -0.9987 ZZ= 180.2892
Eigenvalues: 180.0355 180.0437 189.6646
3 H Isotropic = 32.1402 Anisotropy = 8.8673
XX= 35.0627 YX= -0.7563 ZX= -4.3420
XY= -0.4845 YY= 29.8978 ZY= 0.9262

XZ= -4.2288 YZ= 1.0864 ZZ= 31.4602
Eigenvalues: 28.4309 29.9380 38.0518
4 H Isotropic = 32.1451 Anisotropy = 8.8668
XX= 32.1516 YX= 2.7951 ZX= 3.4871
XY= 2.8369 YY= 30.6113 ZY= 2.3843
XZ= 3.2384 YZ= 2.1709 ZZ= 33.6723
Eigenvalues: 28.4404 29.9387 38.0563
5 H Isotropic = 32.1401 Anisotropy = 8.8770
XX= 29.9484 YX= -0.3121 ZX= 0.4150
XY= -0.6098 YY= 36.2850 ZY= -3.7040
XZ= 0.5540 YZ= -3.6436 ZZ= 30.1870
Eigenvalues: 28.4222 29.9401 38.0581
6 C Isotropic = 183.2100 Anisotropy = 9.7076
XX= 184.6040 YX= -2.7442 ZX= -4.0057
XY= -2.7718 YY= 181.6423 ZY= 2.4292
XZ= -3.9568 YZ= 2.3627 ZZ= 183.3838
Eigenvalues: 179.9530 179.9953 189.6818
7 H Isotropic = 32.1409 Anisotropy = 8.8766
XX= 29.9799 YX= -0.0002 ZX= 0.8926
XY= 0.1160 YY= 29.7298 ZY= 3.2074
XZ= 1.1924 YZ= 3.1297 ZZ= 36.7130
Eigenvalues: 28.4347 29.9293 38.0586
8 H Isotropic = 32.1372 Anisotropy = 8.8693
XX= 35.3780 YX= 3.2618 ZX= -2.7983
XY= 2.9965 YY= 31.1908 ZY= -0.6334
XZ= -2.9139 YZ= -0.7930 ZZ= 29.8428
Eigenvalues: 28.4272 29.9343 38.0500
9 H Isotropic = 32.1394 Anisotropy = 8.8708
XX= 31.5848 YX= -4.2810 ZX= 0.4294
XY= -4.1405 YY= 34.9159 ZY= -1.6918
XZ= 0.2429 YZ= -1.4577 ZZ= 29.9174
Eigenvalues: 28.4275 29.9374 38.0533
10 C Isotropic = 183.2090 Anisotropy = 9.7394
XX= 181.2982 YX= -2.9338 ZX= 1.6489
XY= -2.9925 YY= 186.4200 ZY= -3.5459
XZ= 1.6400 YZ= -3.4711 ZZ= 181.9087
Eigenvalues: 179.9247 180.0002 189.7019
11 H Isotropic = 32.1422 Anisotropy = 8.8593
XX= 33.2319 YX= -4.0391 ZX= -2.5685
XY= -4.1910 YY= 32.5246 ZY= 1.5103
XZ= -2.3749 YZ= 1.2715 ZZ= 30.6701
Eigenvalues: 28.4369 29.9413 38.0484
12 H Isotropic = 32.1459 Anisotropy = 8.8593
XX= 31.8790 YX= 3.2464 ZX= -0.8382
XY= 3.5503 YY= 35.1615 ZY= -2.4218
XZ= -0.9792 YZ= -2.4736 ZZ= 29.3973
Eigenvalues: 28.4425 29.9432 38.0521
13 H Isotropic = 32.1399 Anisotropy = 8.8708
XX= 30.6182 YX= -0.3007 ZX= 4.0215
XY= -0.4617 YY= 29.9186 ZY= -0.3933
XZ= 3.9676 YZ= -0.0963 ZZ= 35.8829

Eigenvalues: 28.4338 29.9321 38.0537
14 C Isotropic = 183.1967 Anisotropy = 9.7548
XX= 181.6819 YX= 1.0858 ZX= 3.5501
XY= 1.0223 YY= 180.5403 ZY= 2.1706
XZ= 3.4803 YZ= 2.2474 ZZ= 187.3679
Eigenvalues: 179.8863 180.0039 189.6999
15 H Isotropic = 32.1386 Anisotropy = 8.8727
XX= 30.4539 YX= -2.4822 ZX= 3.0117
XY= -2.3266 YY= 32.8131 ZY= -2.9624
XZ= 3.0589 YZ= -3.2515 ZZ= 33.1488
Eigenvalues: 28.4308 29.9313 38.0537
16 H Isotropic = 32.1402 Anisotropy = 8.8653
XX= 33.9140 YX= 4.6728 ZX= 0.8605
XY= 4.6386 YY= 32.4070 ZY= 0.5500
XZ= 1.1100 YZ= 0.7600 ZZ= 30.0996
Eigenvalues: 28.4314 29.9388 38.0504
17 H Isotropic = 32.1370 Anisotropy = 8.8804
XX= 31.4714 YX= -1.8102 ZX= -2.5672
XY= -1.9287 YY= 30.2297 ZY= 3.2239
XZ= -2.8656 YZ= 3.2961 ZZ= 34.7100
Eigenvalues: 28.4254 29.9284 38.0573

Average of the Carbon shielding = σ_{TMS} =183.2158

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