Supplementary Material

NMR solution structures of procyanidin B1, B2, and C1

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Figure S1. Top: Conformational analysis of (-)-1b. Small coupling constants of $^{3}J_{H4R,H3} = +4.6$ Hz and $^{3}J_{H4S,H3} = +2.9$ Hz (E-COSY, inset) as well as 1d-pfg-roE response at H4S and H2'/H6' upon irradiation of H2 confirmed the preferred tetrahydropyran-2$H_3$ conformation and conformational flexibility of the catechol; bottom: $^1H$-$^{13}C$-HMBC spectrum of (1b) with $^{3}J_{H3-C10} = 5.5$ Hz, $^{3}J_{H4R-C2} = 0.4$ Hz, and $^{3}J_{H4S-C2}: 5.3$ Hz. Identities of all carbons were established from HMQC correlations and typical one-bond $^1H$-$^{13}C$-J-values were observed.
Figure S2. $^{13}$C NMR of compound 1b

Figure S3. $^1$H-$^1$H-COSY of compound 1b

Figure S4. $^1$H-$^{13}$C-HMQC of compound 1b

Figure S5. No H/D-exchange in compound 1b (H6 and H8).
Figure S6. J-HMBC fitting of compound 1b. Theoretical $J$-values (GIAO, B3LYP/6-311G**(d,p)(u+1s), correction factor$^2$) were Boltzmann-weighted by energy differences between $^2H_3$ and $^3H_2$ half chair for four conformations at 56:26:11:7 (at rt with thermal correction).
Figure S7. Histograms from GAFF-MD-simulation of 1b at rt with explicit methanol solvent. Top: Diagnostic half-chair angle; bottom: distance histogram for H3-H2' and H3H6'.


**Figure S8.** Histogram from MD-simulation of 1b at rt with corresponding Haasnoot-deLeuw-Altona (HLA) equations\(^3\) overlaid.

Equation for H3-C3-C4-H4R (3-substituent system): \[13.22 \cos^2(\phi) - 0.99 \cos(\phi) + \{(0.4 \times (0.87 - 2.46 \times (\cos^2(\phi + 19.9 \times 0.4)) + 1.3 \times (0.87 - 2.46 \times (\cos^2(-\phi + 19.9 \times 1.3)) + 0.4 \times (0.87 - 2.46 \times (\cos^2(\phi + 19.9 \times 0.4))\}.\]

Equation for H3-C3-C4-H4S (3-substituent system): \[13.22 \cos^2(\phi) - 0.99 \cos(\phi) + \{(0.4 \times (0.87 - 2.46 \times (\cos^2(\phi + 19.9 \times 0.4)) + 1.3 \times (0.87 - 2.46 \times (\cos^2(-\phi + 19.9 \times 1.3)) + 0.4 \times (0.87 - 2.46 \times (\cos^2(-\phi + 19.9 \times 0.4))\}.\]

Equation for H2-C2-C3-H3 (4-substituent system): \[13.24 \cos^2(\phi) - 0.91 \cos(\phi) + \{(1.3 \times (0.53 - 2.41 \times (\cos^2(\phi + 15.5 \times 1.3)) + 0.4 \times (0.53 - 2.41 \times (\cos^2(-\phi + 15.5 \times 0.4)) + 1.3 \times (0.53 - 2.41 \times (\cos^2(\phi + 15.5 \times 1.3)) + 0.4 \times (0.53 - 2.41 \times (\cos^2(-\phi + 15.5 \times 0.4))\}.\]
**Compound 1b: Conformer (I) (0.00 kcal/mol)**

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**Compound 1b**: Conformer (III) (+0.96 kcal/mol)

![Structure Diagram]

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**Compound 1b: Conformer (IV) (+1.24 kcal/mol)**

![Compound 1b diagram]

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Figure S9. VT-$^1$H-NMR of compound 2 (methanol-$d_4$).
Figure S10. Direct comparison of $^1$H-spectra of compound 2 – integration at room temperature leads to unreliable results.
Figure S11. Compound 2. Unreliable integration at rt. No apparent change in abundance of species. Therefore, conformational changes between the two species are mostly enthalpy-driven.

Figure S12. CD-Spectrum of native 2 in methanol at room temperature.
Figure S13. $^1$H-$^1$H-COSY of compound 2 at -15 °C

Figure S14. $^1$H-$^{13}$C-HMQC of compound 2 at -15 °C

Figure S15. $^1$H-$^{13}$C-HMBC of compound 2 at -15 °C.

Figure S16. 1d-pfg TOCSY/ROESY of compound 2 at -15 °C.
Figure S17. COSY of compound 2. Minor conformation, ring B.
Figure S18. Histograms from MD-simulation of 2. Top: Diagnostic half-chair dihedral angle in ring A + B at 300 K; bottom: ring A + B at 258 K.
Figure S19. Control experiment: MD-simulation of the (P)-2 atrop isomer at 300 K. No interconversion to the (M)-2 atrop isomer was observed because the rotational barrier was too high. The lowest-energy (P)-structure was +3.81 kcal/mol less stable than the most stable (M)-structure.
Figure S20. Histogram from MD-simulation of 2 at 258 K (-15 °C) with corresponding Haasnoot-deLeuw-Altona (HLA) equations$^3$ overlaid.

Equation for H2â–C2â–C3â–H3â– (4-substituent system): $13.24\cos^2(\varphi) - 0.91\cos(\varphi) + \{(1.3\times(0.53 - 2.41\cos^2(\varphi + 15.5\times1.3)) + 0.4\times(0.53 - 2.41\cos^2(-\varphi + 15.5\times0.4)) + 1.3\times(0.53 - 2.41\cos^2(\varphi + 15.5\times1.3)) + 0.4\times(0.53 - 2.41\cos^2(-\varphi + 15.5\times0.4))\}.$

Equation for H3â–C3â–C4â–H4â– (4-substituent system): $13.24\cos^2(\varphi) - 0.91\cos(\varphi) + \{(0.4\times(0.53 - 2.41\cos^2(\varphi + 15.5\times0.4)) + 1.3\times(0.53 - 2.41\cos^2(-\varphi + 15.5\times1.3)) + 0.4\times(0.53 - 2.41\cos^2(-\varphi + 15.5\times0.4))\}.$

Equation for H2â–C2â–C3â–H3â– (4-substituent system): $13.24\cos^2(\varphi) - 0.91\cos(\varphi) + \{(1.3\times(0.53 - 2.41\cos^2(\varphi + 15.5\times1.3)) + 0.4\times(0.53 - 2.41\cos^2(-\varphi + 15.5\times0.4)) + 1.3\times(0.53 - 2.41\cos^2(-\varphi + 15.5\times1.3)) + 0.4\times(0.53 - 2.41\cos^2(-\varphi + 15.5\times0.4))\}.$

Equation for H3â–C3â–C4â–H4â– (3-substituent system): $13.22\cos^2(\varphi) - 0.99\cos(\varphi) + \{(1.3\times(0.87 - 2.46\cos^2(\varphi + 19.9\times1.3)) + 0.4\times(0.87 - 2.46\cos^2(-\varphi + 19.9\times0.4)) + 1.3\times(0.87 - 2.46\cos^2(-\varphi + 19.9\times1.3)) + 0.4\times(0.87 - 2.46\cos^2(-\varphi + 19.9\times0.4))\}.$

Equation for H3â–C3â–C4â–H4â– (3-substituent system): $13.22\cos^2(\varphi) - 0.99\cos(\varphi) + \{(1.3\times(0.87 - 2.46\cos^2(\varphi + 19.9\times1.3)) + 0.4\times(0.87 - 2.46\cos^2(-\varphi + 19.9\times0.4)) + 1.3\times(0.87 - 2.46\cos^2(-\varphi + 19.9\times1.3)) + 0.4\times(0.87 - 2.46\cos^2(-\varphi + 19.9\times0.4))\}.$
; Definition of sample heteronuclear spin system
; C-CH2-CH-CH
;
proton  a 2.575  t= 0.3
proton  b 2.596  t= 0.3
proton  c 4.12  t= 0.4
proton  d 4.905  t= 0.3
;
; H-H couplings in Hz
;
couple  a b -17.0
couple  a c 5.9
couple  b c 4.5
couple  c d 5

Figure S21. Parameters for the simulation of the spin system H2-H3-H4R/S in NMRSim 6.0 (TopSpin 3.5 pl7) (Bruker).
Compound 2: Conformer (I) (0.00 kcal/mol) – Five H-bonds
Compound 2: Conformer (II) (+0.45 kcal/mol) – Four H-bonds

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©ARKAT USA, Inc
**Compound 2:** Conformer (III) (+0.70 kcal/mol) – Three H-bonds
**Compound 2**: Conformer (IV) (+0.90 kcal/mol) – Three H-bonds
Figure S22. Compound 3. Unreliable integration at rt. No apparent change in abundance of species. Therefore, conformational changes between the two species are mostly enthalpy-driven.

Figure S23. The CD-spectrum of native 3 in methanol at room temperature.
Figure S24. $^1$H-$^1$H-COSY of compound 3 at -15 °C

Figure S25. $^1$H-$^{13}$C-HMQC of compound 3 at -15 °C

Figure S26. $^1$H-$^{13}$C-HMBC of compound 3 at -15 °C.

Figure S27. 1d-pfg TOCSY of compound 3 at -15 °C.
Figure S28. 1d-pfg-TOCSY + ROESY of compound 3 at -15 °C
Figure S29. Histograms from MD-simulation of 3. Top: Diagnostic half-chair dihedral angle in ring A + B at 300 K; bottom: ring A + B at 258 K.
Figure S30. Control experiment: MD-simulation of the \((P)\)-3 atrop isomer at 300 K. No interconversion to the \((M)\)-3 atrop isomer was observed because the rotational barrier was too high. The lowest-energy \((P)\)-structure was +3.40 kcal/mol less stable than the most stable \((M)\)-structure.
Figure S31. Histogram from MD-simulation of 3 at 258 K (-15 °C) with corresponding Haasnoot-deLeuw-Altona (HLA) equations\(^3\) overlaid.

Equation for H2A-C2A-C3A-H3A (4-substituent system) and for H2B-C2B-C3B-H3B (4-substituent system): \[13.24 \cos^2(\varphi) - 0.91 \cos(\varphi) + \{[1.3 \times (0.53 - 2.41 \cos^2(\varphi + 15.5 \times 1.3)) + 0.4 \times (0.53 - 2.41 \cos^2(-\varphi + 15.5 \times 0.4)) + 1.3 \times (0.53 - 2.41 \cos^2(\varphi + 15.5 \times 1.3)) + 0.4 \times (0.53 - 2.41 \cos^2(-\varphi + 15.5 \times 0.4))\}\].

Equation for H3A-C3A-C4A-H4A (4-substituent system): \[13.24 \cos^2(\varphi) - 0.91 \cos(\varphi) + \{[0.4 \times (0.53 - 2.41 \cos^2(\varphi + 15.5 \times 0.4)) + 1.3 \times (0.53 - 2.41 \cos^2(-\varphi + 15.5 \times 1.3)) + 0.4 \times (0.53 - 2.41 \cos^2(-\varphi + 15.5 \times 0.4))\}\].

Equation for H3B-C3B-C4B-H4BR (3-substituent system): \[13.22 \cos^2(\varphi) - 0.99 \cos(\varphi) + \{[1.3 \times (0.87 - 2.46 \cos^2(\varphi + 19.9 \times 1.3)) + 0.4 \times (0.87 - 2.46 \cos^2(-\varphi + 19.9 \times 0.4)) + 0.4 \times (0.87 - 2.46 \cos^2(-\varphi + 19.9 \times 0.4))\}\].

Equation for H3B-C3B-C4B-H4BS (3-substituent system): \[13.22 \cos^2(\varphi) - 0.99 \cos(\varphi) + \{[1.3 \times (0.87 - 2.46 \cos^2(\varphi + 19.9 \times 1.3)) + 0.4 \times (0.87 - 2.46 \cos^2(-\varphi + 19.9 \times 0.4)) + 0.4 \times (0.87 - 2.46 \cos^2(-\varphi + 19.9 \times 0.4))\}\].
Compound 3: Conformer (I) (0.00 kcal/mol) – Four H-bonds
**Compound 3:** Conformer (II) (+0.23 kcal/mol) – Four H-bonds

![Molecular structure](image)

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**Compound 3**: Conformer (III) (+0.78 kcal/mol) – Four H-bonds

![Diagram of Compound 3 with H-bonds]
**Compound 3:** Conformer (IV) (+ 0.98 kcal/mol) – Four H-bonds
Figure S32. VT-\(^1\)H-NMR of compound 4 at -15 \(^\circ\)C.

Figure S33. \(^1\)H-NMR + 1d-pfg-tcosy of compound 4 at -15 \(^\circ\)C.

Figure S34. \(^1\)H-\(^1\)H-COSY of compound 4 at -15 \(^\circ\)C.

Figure S35. \(^1\)H-\(^{13}\)C-HMQC of compound 4 at -15 \(^\circ\)C.
Figure S36. $^1$H-$^{13}$C-HMBC of compound 4 at -15 °C.
Figure S37. 1d-pfg-ROESY of compound 4 at -15 °C (methanol-d₄)
Figure S38. Compound 4. Unreliable integration at rt. No apparent change in abundance of species. Therefore, conformational changes between the two species are mostly enthalpy-driven.

Figure S39. CD-Spectrum of native 4 in methanol at room temperature.
Figure S40. Histograms from MD-simulation of 4. Top: Diagnostic half-chair dihedral angle in ring A + B + C at 300 K; bottom: ring A + B + C at 258 K.
Figure S41. Histogram from MD-simulation of 4 at 258 K (-15 °C) with corresponding Haasnoot-deLeuw-Altona (HLA) equations\(^3\) overlaid.

Equation for H2^A^-C2^A^-C3^A^-H3^A (4-substituent system), for H2^B^-C2^B^-C3^B^-H3^B (4-substituent system), and for H2^C^-C2^C^-C3^-H3^C (4-substituent system): 13.24*cos^2(\(\phi\)) - 0.91*cos(\(\phi\)) + \{[1.3*(0.53 - 2.41*(\cos^2(\(\phi\) + 15.5*1.3)))] + 0.4*(0.53 - 2.41*(\cos^2(-\(\phi\) + 15.5*0.4)))] + 1.3*(0.53 - 2.41*(\cos^2(\(\phi\) + 15.5*1.3)))] + 0.4*(0.53 - 2.41*(\cos^2(-\(\phi\) + 15.5*0.4))].

Equation for H3^A^-C3^A^-C4^A^-H4^A (4-substituent system) and for H3^B^-C3^B^-C4^B^-H4^B (4-substituent system): 13.24*cos^2(\(\phi\)) - 0.91*cos(\(\phi\)) + \{[0.4*(0.53 - 2.41*(\cos^2(\(\phi\) + 15.5*0.4)))] + 1.3*(0.53 - 2.41*(\cos^2(-\(\phi\) + 15.5*1.3)))] + 0.4*(0.53 - 2.41*(\cos^2(-\(\phi\) + 15.5*0.4))].

Equation for H3^C^-C3^C^-C4^-H4^R (3-substituent system): 13.22*cos^2(\(\phi\)) - 0.99*cos(\(\phi\)) + \{[1.3*(0.87 - 2.46*(\cos^2(\(\phi\) + 19.9*1.3)))] + 0.4*(0.87 - 2.46*(\cos^2(-\(\phi\) + 19.9*0.4))].

Equation for H3^C^-C3^C^-C4^-H4^S (3-substituent system): 13.22*cos^2(\(\phi\)) - 0.99*cos(\(\phi\)) + \{[1.3*(0.87 - 2.46*(\cos^2(\(\phi\) + 19.9*1.3)))] + 0.4*(0.87 - 2.46*(\cos^2(-\(\phi\) + 19.9*0.4))].
**Compound 4: Conformer (I) (0.00 kcal/mol) – Six H-bonds**
Compound 4: Conformer (II) (0.25 kcal/mol) – Six H-bonds
Compound 4: Conformer (III) (1.22 kcal/mol) – Seven H-bonds
Compound 4: Conformer (IV) (1.76 kcal/mol) – Seven H-bonds
**Compound 4:** Conformer (V) (2.19 kcal/mol) – Six H-bonds
**Compound 4: Conformer (VI) (2.22 kcal/mol) – Seven H-bonds**
## Compound 4: Conformer (VII) (2.63 kcal/mol) – Seven H-bonds

![Conformer VII](image)

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Table 1. $^{13}$C-NMR chemical shifts in ppm for (-)-epicatechin (1), procyanidin B1 (2), B2 (3), and C1 (4) in MeOD. Compound 1 was measured at rt; compounds 2-4 were measured at -15 °C. $^a$$\delta$ = 155-157 ppm (C5$^{A,B}$, C7$^{A,B}$, C9$^{A,B}$; not resolved, ambiguous), $^b$$\delta$ = 143-145 ppm (C3'$^{A,B}$, C4'$^{A,B}$; not resolved, ambiguous), $^c$$\delta$ = 154-157 ppm (C5$^{A,B,C}$, C7$^{A,B,C}$, C9$^{A,B,C}$; not resolved, ambiguous), $^d$$\delta$ = 143-145 ppm (C3'$^{A,B,C}$, C4'$^{A,B,C}$; not resolved, ambiguous).

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