Supporting Information

Kinetics and Equilibria of Cis/Trans Isomerization of Backbone Amide Bonds in Peptoids

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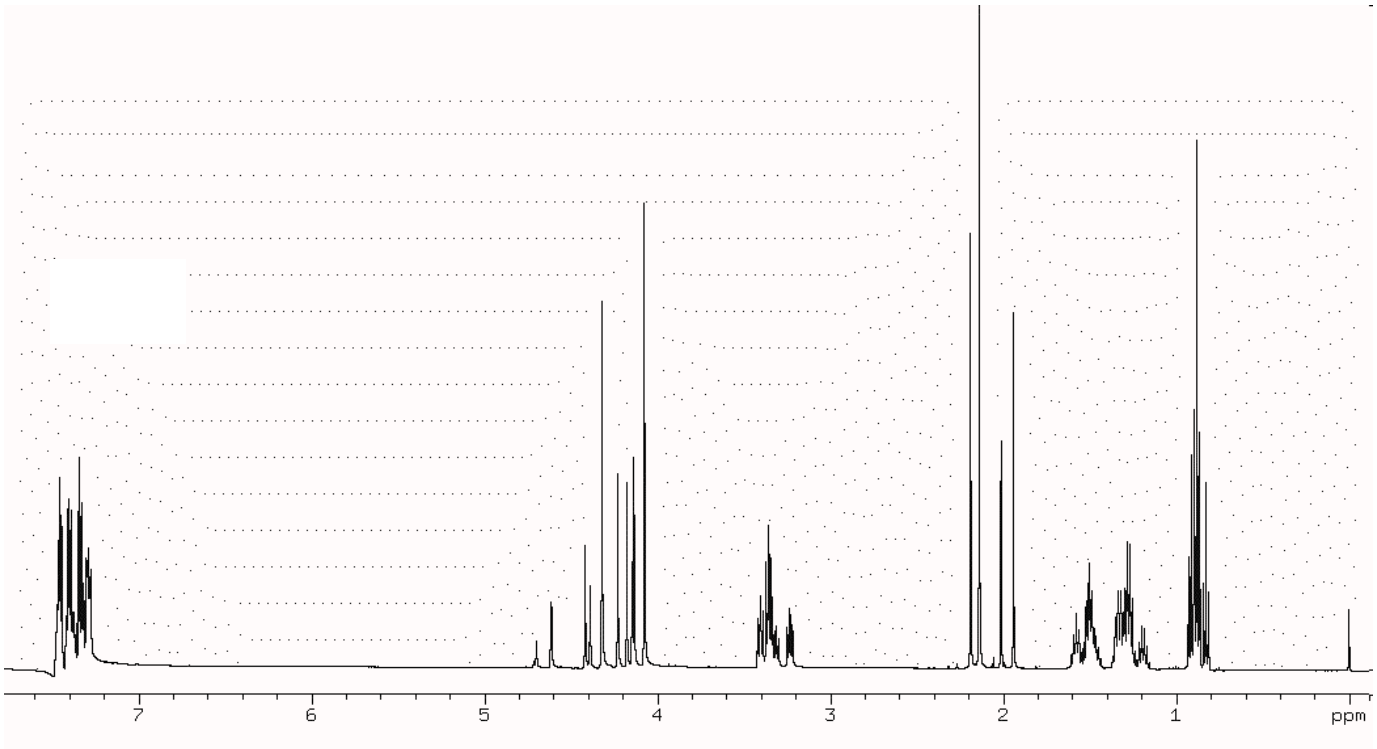

Figure S1. 1D ^{1}H NMR spectrum of 8.2 mM Ac-N(butyl)-N(benzyl)-NH_2 (peptoid **3**) in 100% D_2O, pD 2.8 and 25ºC.

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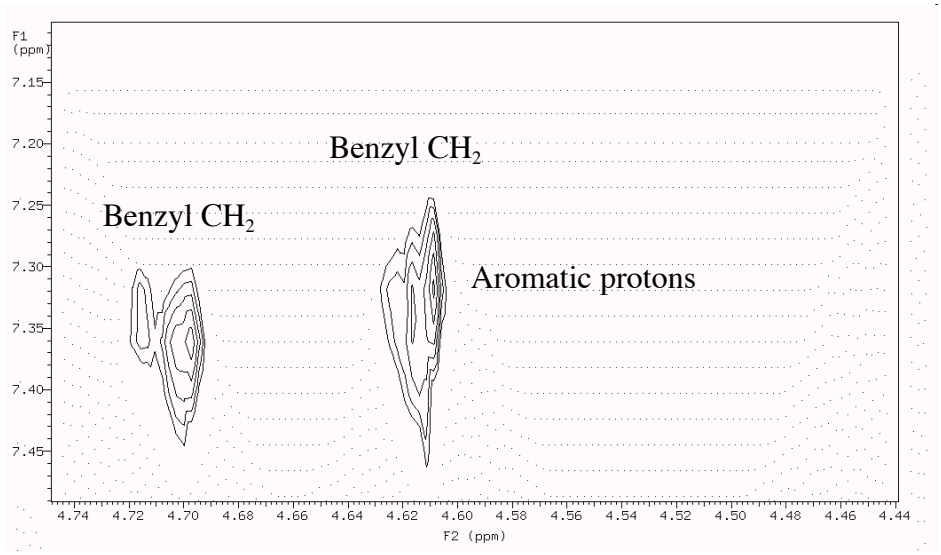

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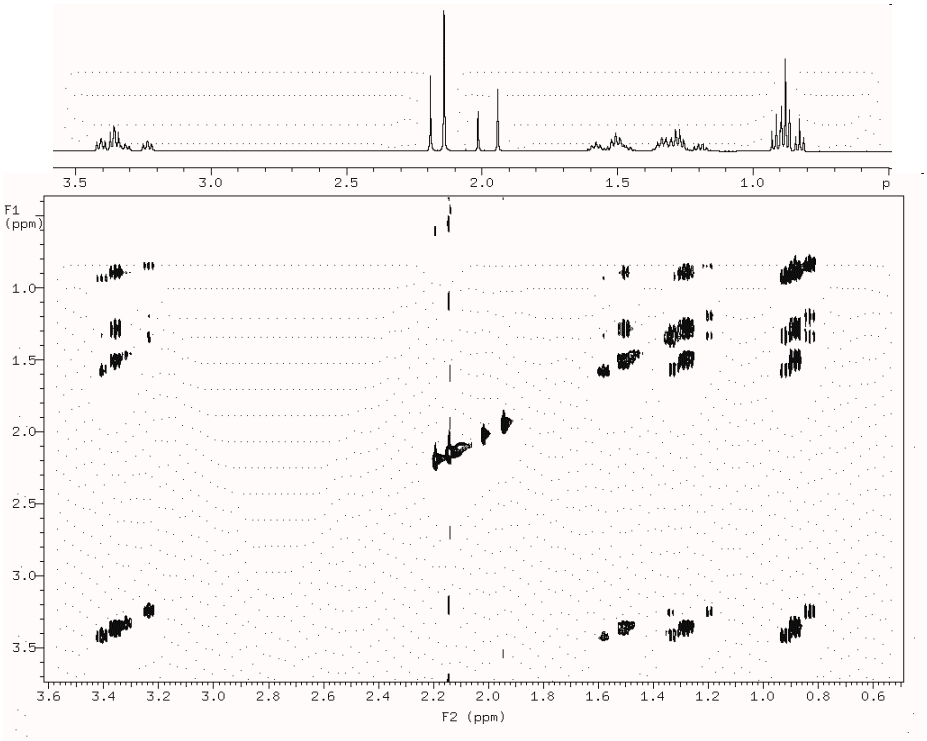
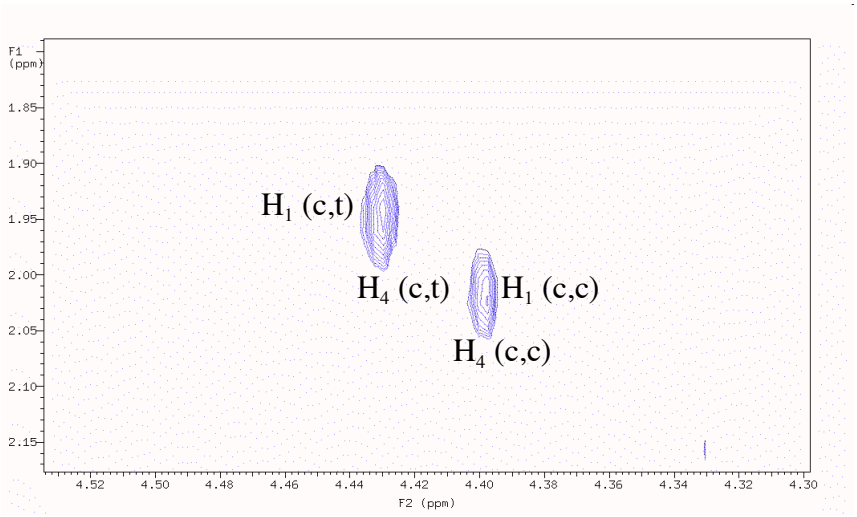


Figure S2. Portions of the TOCSY spectrum of 8.2 mM Peptoid **3** in 100% D_2O, pD 2.8 and 25ºC. (A) shows cross peaks between benzyl CH_2 resonances (4.61 and 4.71 ppm) and aromatic proton resonances (7.28–7.36 ppm). (B) This portion of the TOCSY spectrum shows cross peaks between the n-butyl side chain resonances; the 1D spectrum is shown on the top of the TOCSY spectrum.

A



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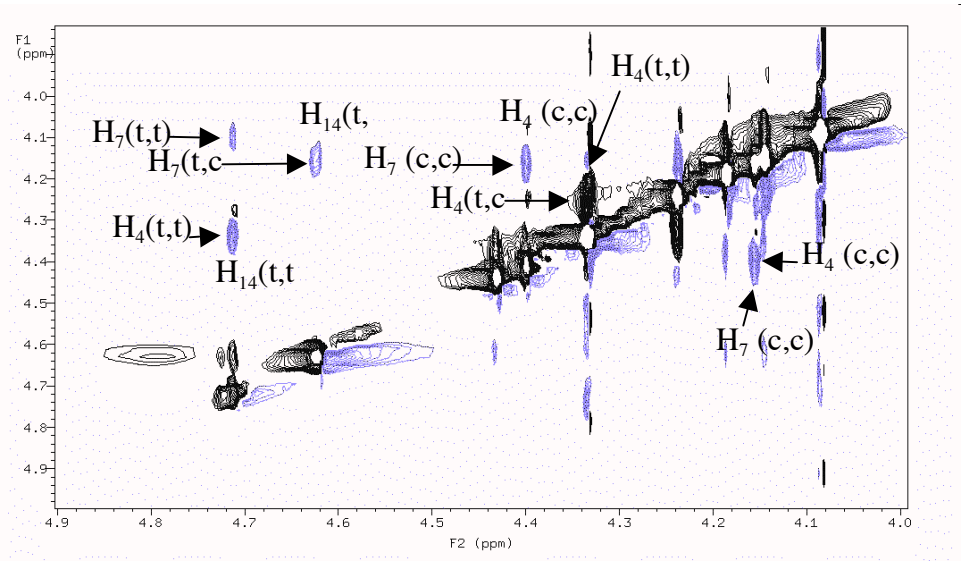

Figure S3. (A) A portion of the negative-contoured ROESY spectrum of 8.2 mM Ac-N(butyl)-NH_2 in 100% D_2O, pD 2.8 and 25ºC shows cross peaks between resonances of H_1(c,t) and H_4(c,t), and between resonances of H_1(c,c) and H_4(c,c). Mixing time was 120ms; (B) ROESY spectrum shows the correlations between H_4(c,c) and H_7(c,c) resonances. Both positive and negative contours are plotted.

Table S1. Assignment of the ^{1}H NMR spectrum of Peptoid **3**[a]

Proton	(t, t)	(t, c)	(c, t)	(c, c)
H_1	2.139	2.189	1.941	2.013
H_4	4.321	4.228	4.418	4.389
H_7	4.076	4.135	4.177	4.147
H_{14}	4.70	4.61	4.717	4.62
H_{10}	3.37	3.42	3.23	3.32
H_{11}	1.51	1.58	1.34	1.50
H_{12}	1.28	1.33	1.19	1.28
H_{13}	0.88	0.92	0.82	0.88

[a]Units in ppm.

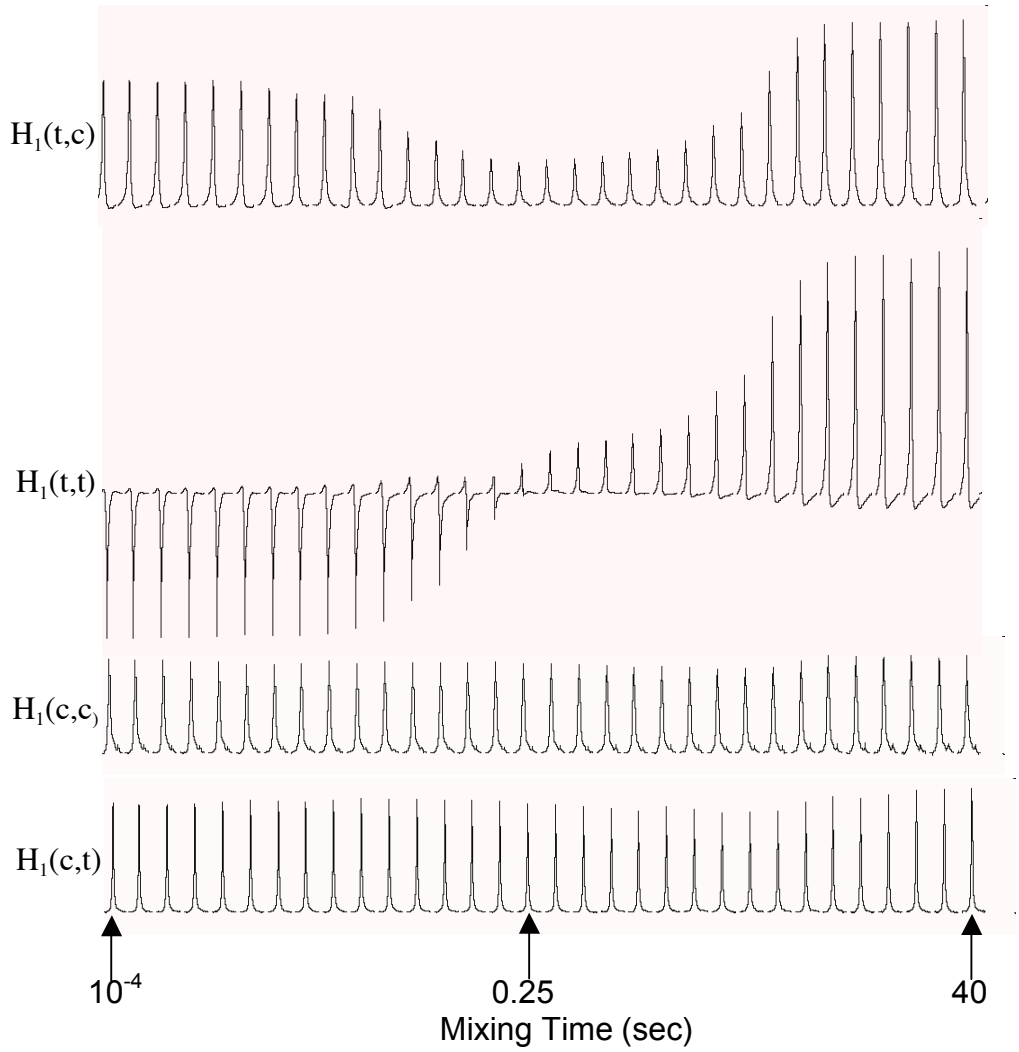

Figure S4. Intensities of resonances for the acetyl protons of the four isomers of Peptoid **3** after selectively inverting the resonance for H_1(t,t) with the DANTE inversion magnetization transfer pulse sequence followed by variable mixing times. The temperature was 55ºC. The resonance for H_1(t,c) shows a dip in intensity while the resonances for H_1(c,c) and H_1(c,t) do not, which indicates chemical exchange happens only between H_1(t,c) and H_1(t,t) on the inversion-magnetization transfer NMR time scale. The time scale is not linear; the mixing times are as follows: 0.0001, 0.0002, 0.0004, 0.0008, 0.001, 0.002, 0.004, 0.008, 0.01, 0.02, 0.04, 0.08, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4, 0.45, 0.5, 0.6, 0.8, 1, 2, 4, 8, 10, 15, 20, 30 and 40 sec.

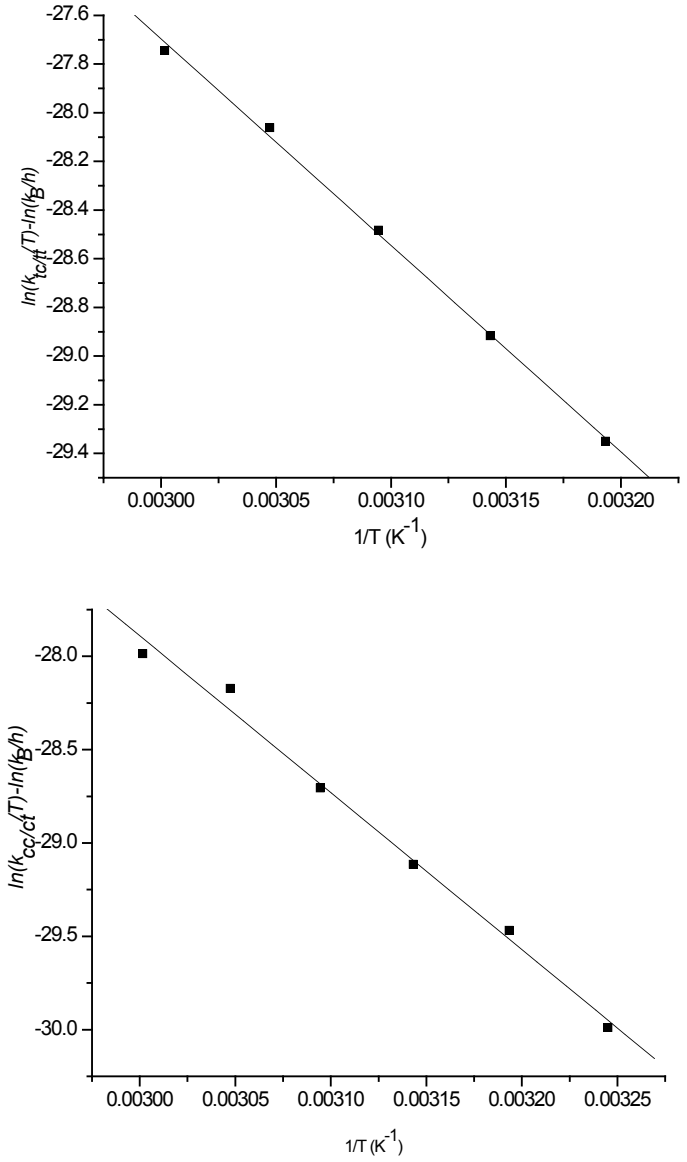

Figure S5. Eyring plots of (Top) $\ln(k_{tc/tt}/T)-\ln(k_B/T)$ vs 1/T for H_1(t,c) and (Bottom) $\ln(k_{cc/ct}/T)-\ln(k_B/T)$ vs 1/T for H_1(c,c), where $k_{tc/tt}$ is the rate constant for (t,c)→ (t,t) reaction, and $k_{cc/ctt}$ is the rate constant for (c,c)→ (c,t) reaction.

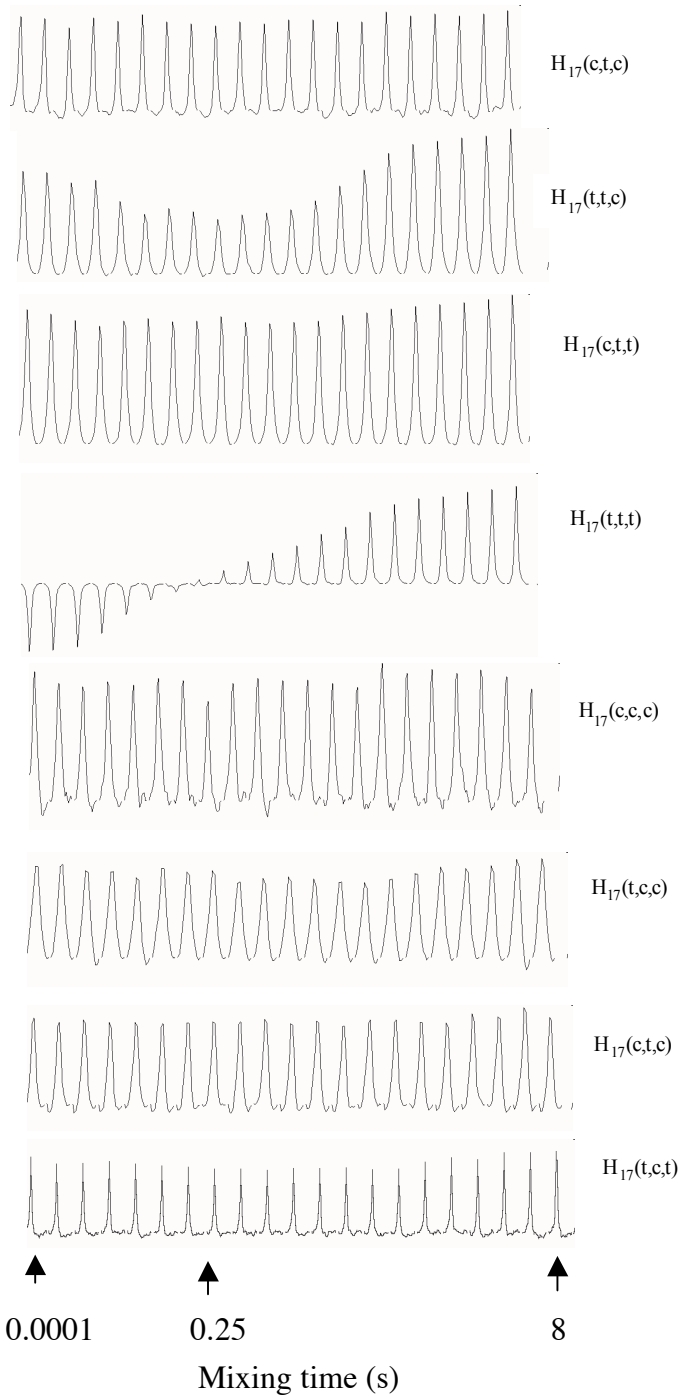

Figure S6. Intensities of resonances for the methyl protons (H_{17}) of the eight isomers of Peptoid **7** after selectively inverting the resonance for H_{17}(t,t,t) at 55ºC with the DANTE inversion-magnetization transfer pulse sequence followed by variable mixing times. The H_{17}(t,t,c) resonance shows a dip in the arrayed resonances while other resonances barely show any, which indicates that transfer of magnetization by chemical exchange happens only between H_{17}(t,t,c) and H_{17}(t,t,t) on the NMR scale. The mixing time is as follows: 0.0001, 0.001, 0.01, 0.05, 0.1, 0.15, 0.2, 0.25, 0.3, 0.4, 0.5, 0.6, 0.8, 1, 1.5, 2, 2.5, 3, 4, 5, 8 sec.

Table S2. Activation parameters for cis-to-trans interchange, e.g. for (t,c)-to-(t,t).

Peptoid	Rate Constant	$\Delta H^{\ddagger}$,kcal mol^{-1}	$\Delta S^{\ddagger}$, cal K^{-1} mol^{-1}	$\Delta G^{\ddagger}$,kcal mol^{-1}
1	$k_{c/t}$	14.5±0.5	-15.0±1.4	19.0±0.9
2	$k_{c/t}$	12.9±0.4	-20.0±0.7	18.9±0.6
3	$k_{tc/tt}$	18.7±1	-5±2	18±2
3	$k_{cc/ct}$	16.7±0.8	1±3	18.3±1.5
4	$k_{tc/tt}$	18.6±0.9	0.6±3	18±2
4	$k_{cc/ct}$	16.1±0.4	-7±1.5	18.2±0.1
5	$k_{cc/ct}$	20±2	2±2	19.4±2.5
6	$k_{tc/tt}$	13.9±0.9	-14±2	18.1±1.5
6	$k_{cc/ct}$	15.0±2	-11±5	18.5±3
7	$k_{ttc/ttt}$	15.6±0.6	-10±2	18±1
7	$k_{ctc/ctt}$	19.7±0.8	2.5±0.3	19±0.3
7	$k_{ccc/cct}$	16±1	-6±3	17.8±1.8
7	$k_{tcc/tct}$	21±2	8±5	19±3