Examination of pinanediol - boronic acid ester formation in aqueous media: relevance to the relative stability of trigonal and tetrahedral boronate esters

Mayte A. Martínez-Aguirre, Marcos Flores-Alamo, Felipe Medrano and Anatoly K. Yatsimirsky*

Supporting information

Index

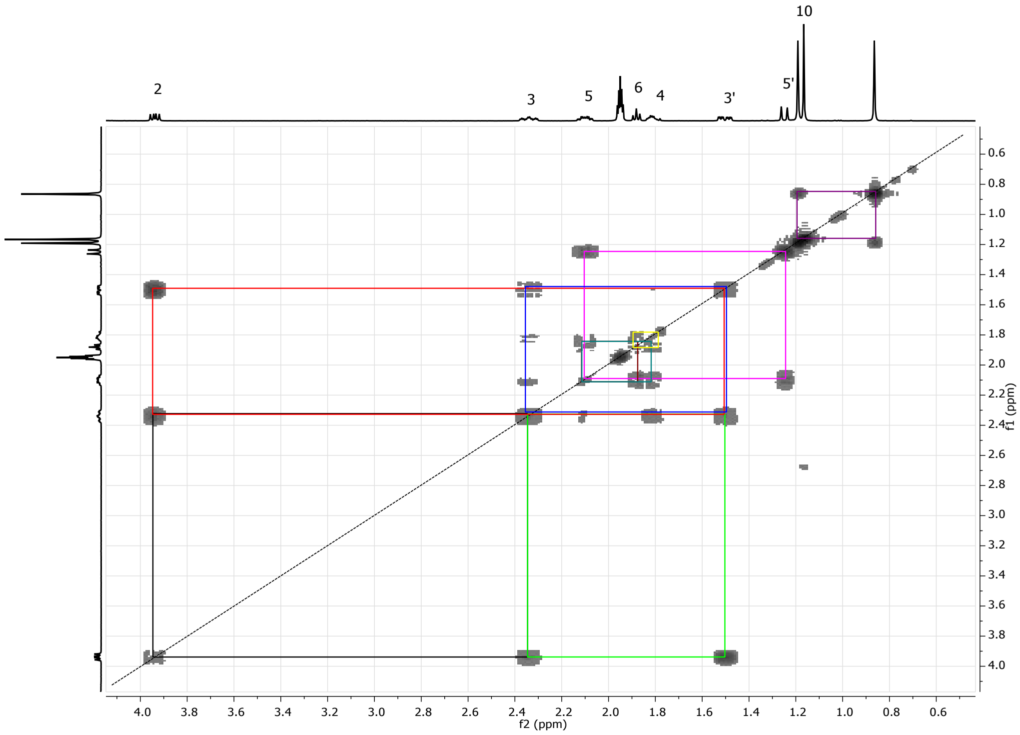


Figure S1. COSY spectra (400 MHz, 40% v/v MeCN-d_3/D_2O) of (-)-pinanediol.

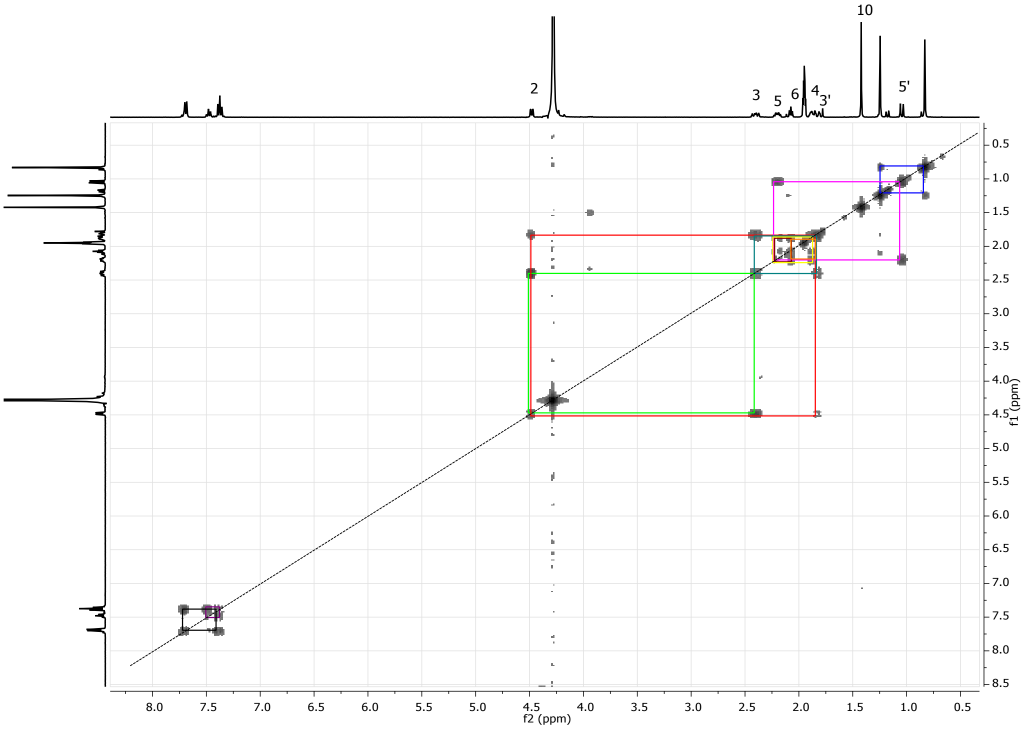


Figure S2. COSY spectra (400 MHz, 40% v/v MeCN-d_3/D_2O) of equimolar mixture of PBA and (-)-pinanediol.

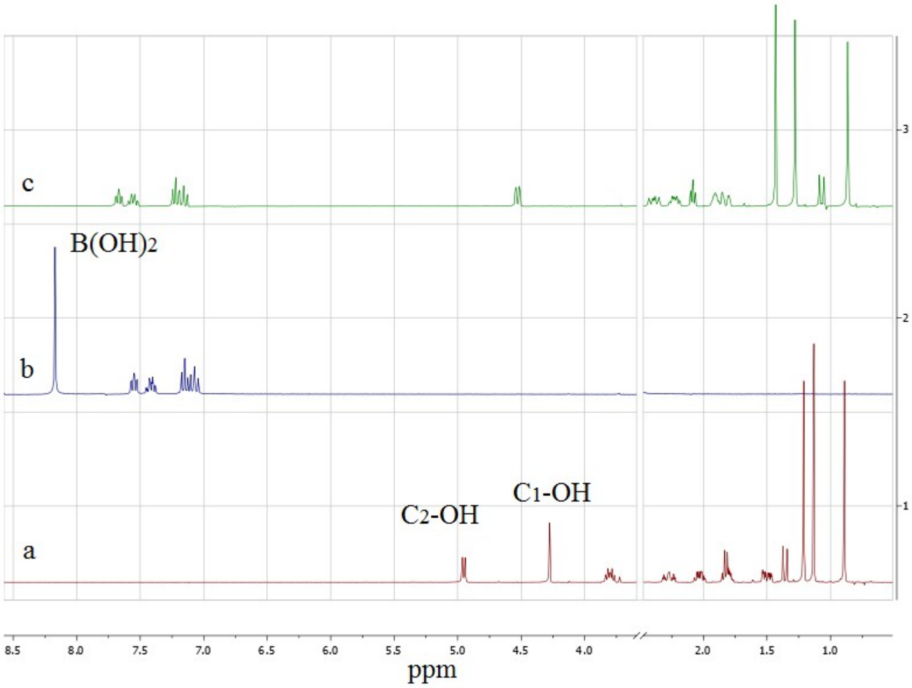


Figure S3. ^{1}H NMR spectra (300 MHz) of 5 mM pinanediol (a), FPBA (b) and their 1:1 mixture (c) in DMSO-d_6.

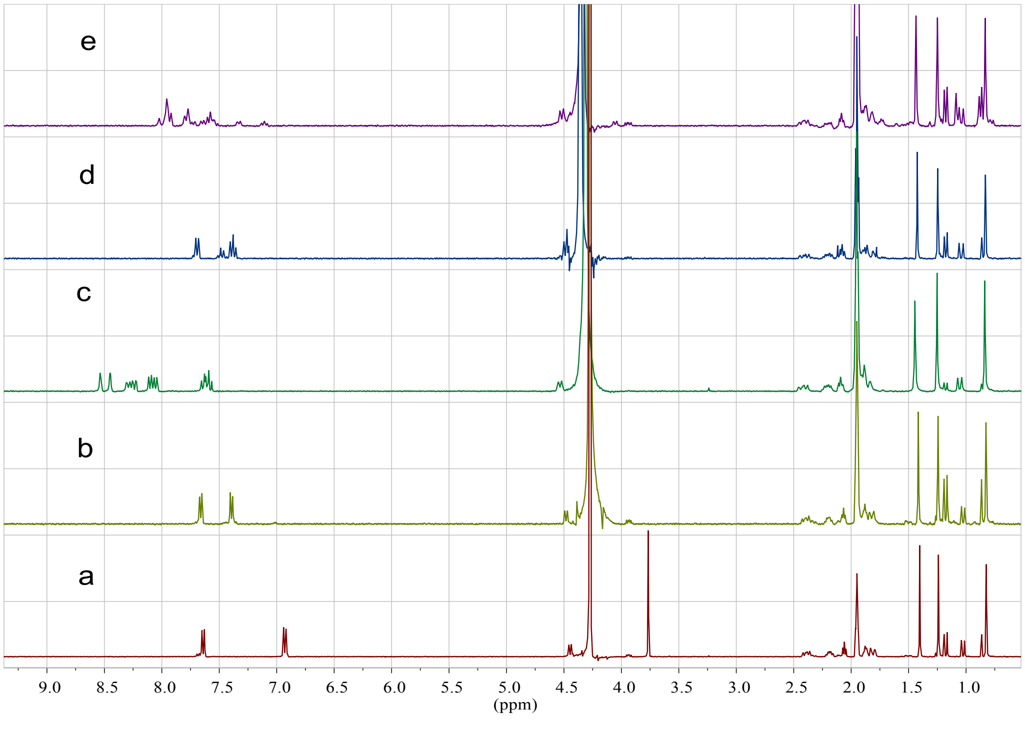


Figure S4. ^{1}H NMR spectra for the equimolar mixture (2-5 mM) of pinanediol and boronic acids (a) 4-MeO, (b) 4-Cl, (c) 3-NO_3, (d) H (PBA), (e) 3-CF_3 in 40% v/v MeCN-d_3/D_2O.

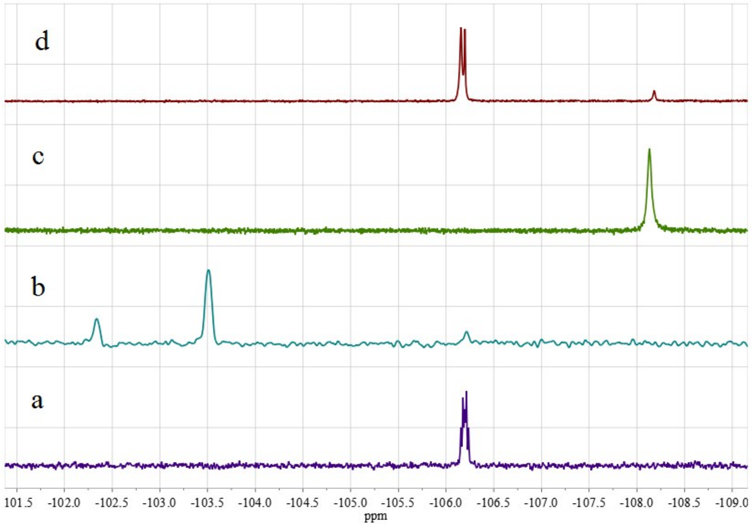


Figure S5. ^{19}F NMR spectra of free 5 mM FPBA (a), the equimolar mixture of FPBA-pinanediol without added base (b), 6 mM FPBA in the presence of 1 equivalent of NaOH (c), mixture of 6 mM FPBA and 6.9 mM pinanediol in the presence of 6 mM of NaOH (d) obtained in 40% v/v MeCN-d_3/D$_2$O at 282 MHz.

Figure S5(a) shows the ^{19}F NMR spectrum of free FPBA in a neutral solution with signal at -106.19 ppm. In the presence of 1 molar equivalent of pinanediol, spectrum (b), two additional signals at -103.50 and -102.34 ppm appear due to formation of the trigonal ester. The observation of two peaks can be explained by formation of slowly interchanging in the NMR time scale two isomeric esters with *ortho*-F atom positioned in front of either 10-Me or 2-CH groups of pinanediol. The integration of these signals gives the overall value of $K_{\text{trig}} = 1.8\times10^4$ M^{-1}. The spectrum (c) shows the signal of FPBA anion at -108.13 ppm. In the presence of a small excess of pinanediol, spectrum (d), two additional peaks at -106.19 and -106.16 ppm appear due to formation of the tetrahedral isomeric esters with overall $K_{\text{tet}} = 4500$ M^{-1} value calculated by the integration of the signals.

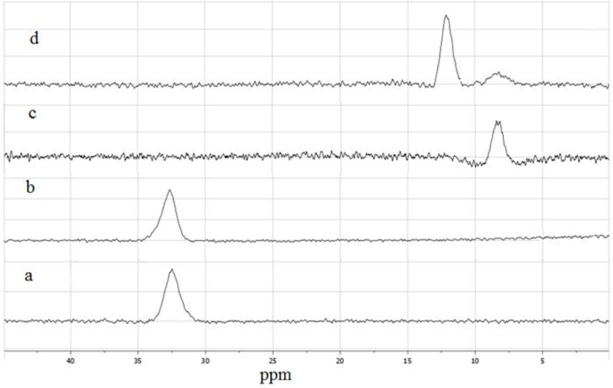


Figure S6. ^{11}B NMR spectra (160 MHz) of 5 mM free benzoxaborole (a), the equimolar mixture of benzoxaborole-pinanediol (b), benzoxaborole in the presence of 1 equivalent of NaOH (c) and the equimolar mixture of benzoxaborole-pinanediol in the presence of 1 equivalent of NaOH (d) obtained in 40% v/v MeCN-d_3/D_2O.

Figure S6(a) shows the ^{11}B NMR spectrum of free benzoxaborole in a neutral solution with signal at 32.46 ppm. In the presence of 1 molar equivalent of pinanediol, spectrum (b), the signal shifts to 32.64 ppm due to formation of the trigonal ester. Addition of 1 molar equivalent of hydroxide to this mixture transforms the spectrum in that shown in figure S6d with well resolved signals at 12.17 and 8.28 ppm. The signal at 8.28 ppm belongs to the free anion of benzoxaborole, as is evident from the spectrum (c).

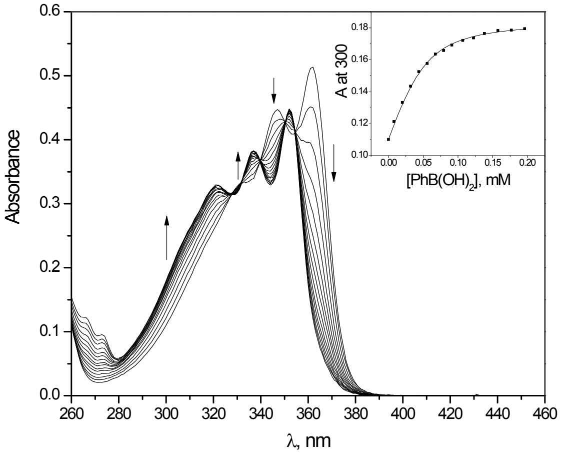


Figure S7. Spectrophotometric titration of 50 μM chromotropic acid by phenylboronic acid at pH 7 (50 mM MOPS buffer). Arrow shows the direction of spectral changes induced by increased $PhB(OH)_2$ concentrations. Inset shows the titration profile at a single wavelength and its fitting to the equation (1).

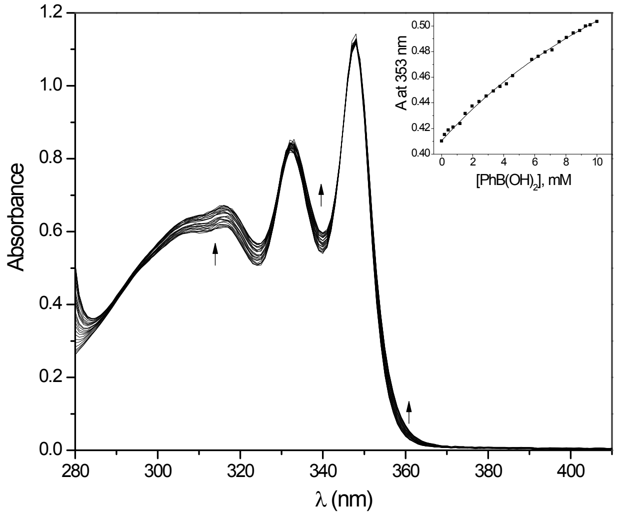


Figure S8. Spectrophotometric titration of 100 μM chromotropic acid by phenylboronic acid at pH 1. Arrow shows the direction of spectral changes induced by increased PhB(OH)$_2$ concentrations. Inset shows the titration profile at a single wavelength and its fitting to the equation (1).

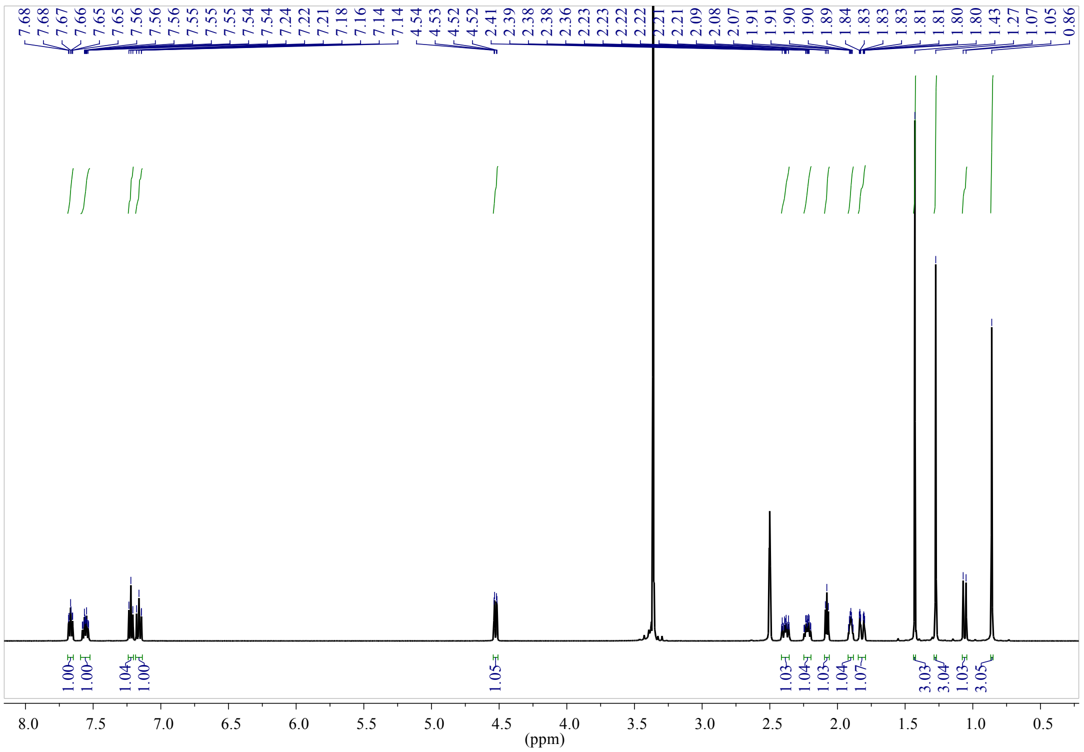


Figure S9. ^{1}H NMR spectra (500 MHz, DMSO-d_6) of boronate ester **2**.

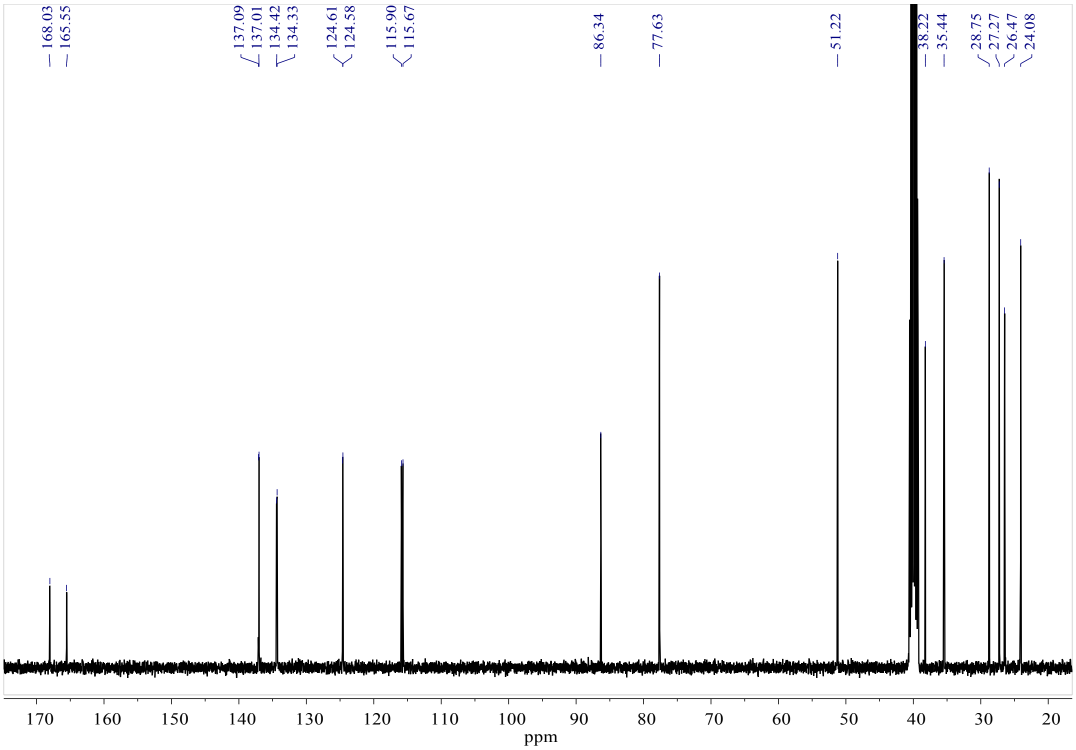


Figure S10. ^{13}C NMR spectra (101 MHz, DMSO-d_6) of boronate ester **2**.

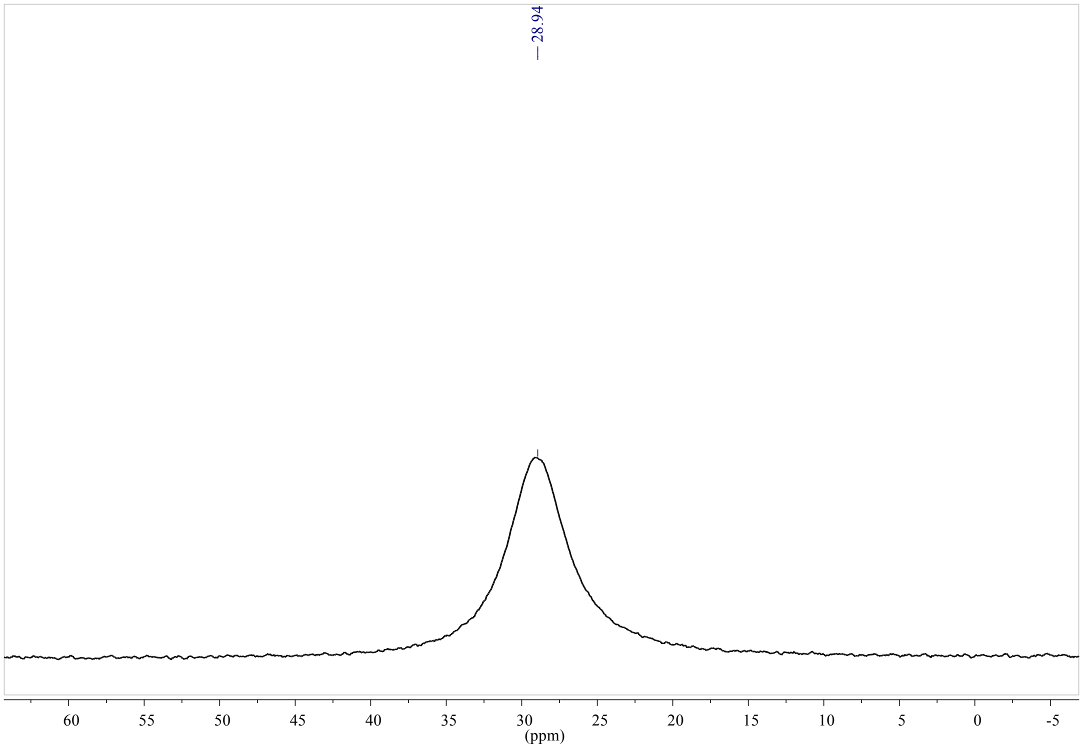


Figure S11. ^{11}B NMR spectra (160 MHz, DMSO-d_6) of boronate ester **2**.

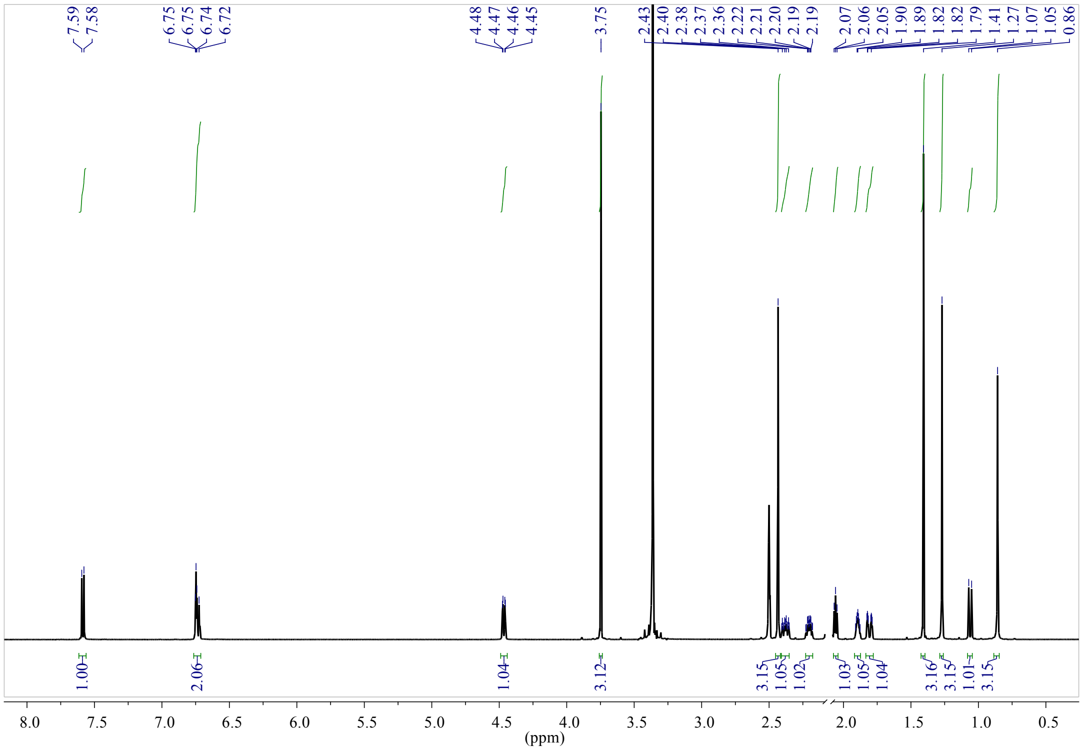


Figure S12. ^{1}H NMR spectra (500 MHz, DMSO-d_6) of boronate ester **3**.

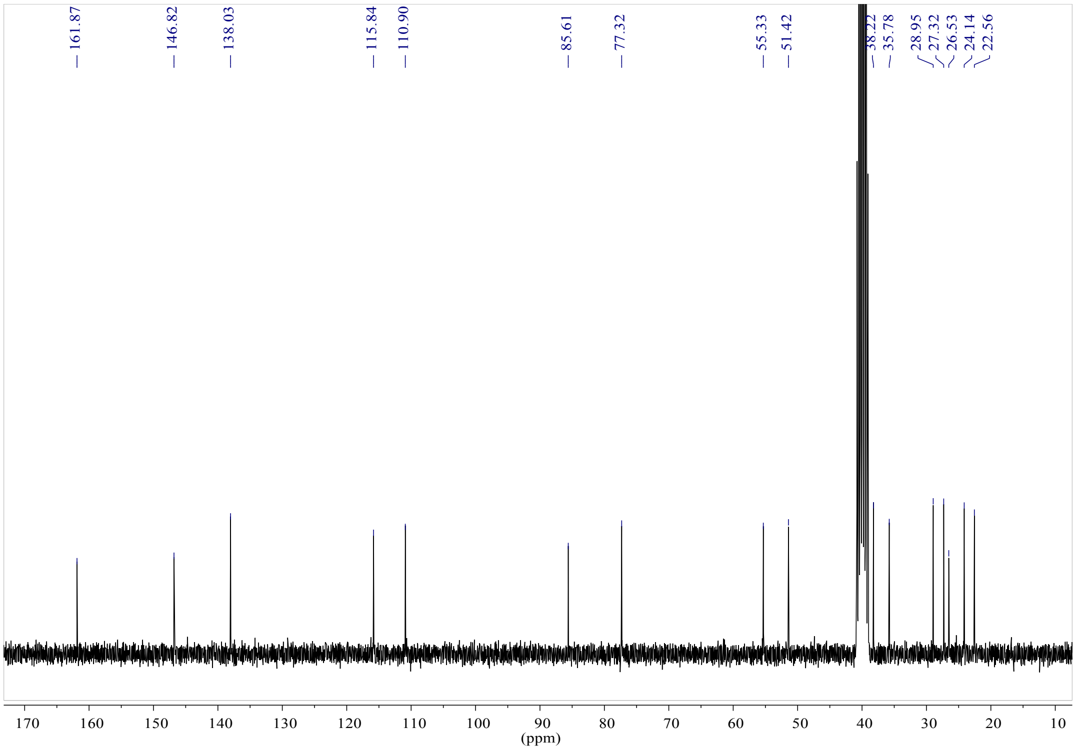


Figure S13. ^{13}C NMR spectra (75MHz, DMSO-d_6) of boronate ester **3**.

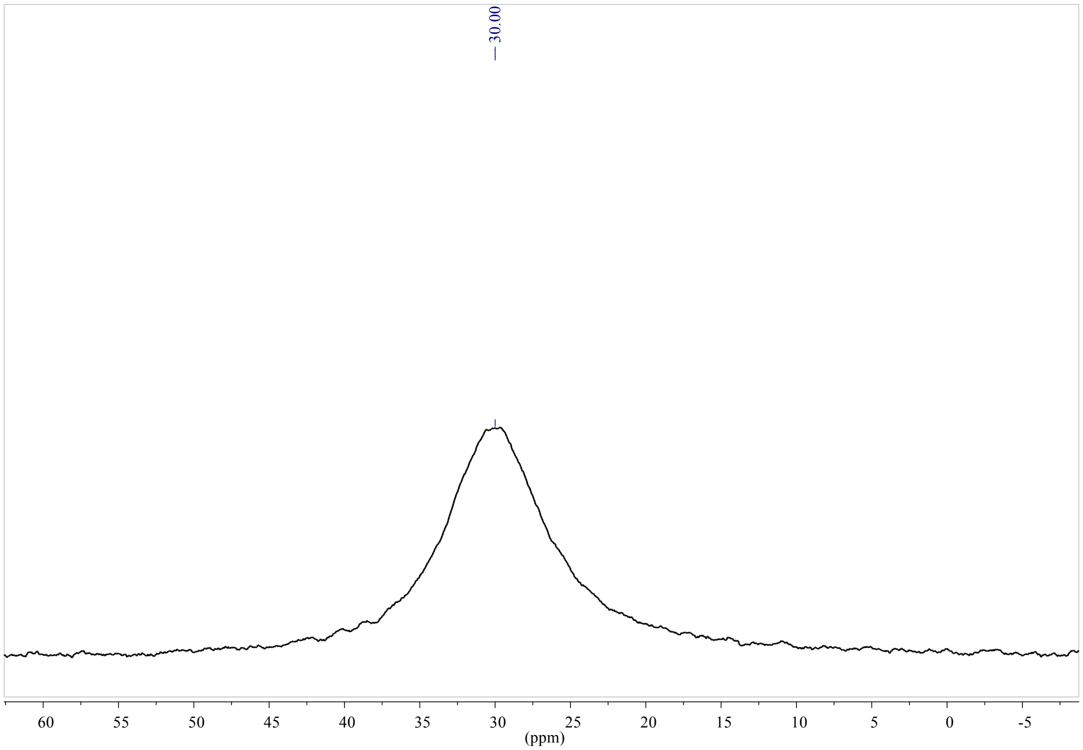


Figure S14. ^{11}B NMR spectra (160 MHz, DMSO-d_6) of boronate ester **3**.

Table S1. Crystallographic data for compounds **2** and **3**.

Identification code	**2**	**3**
Empirical formula	C16 H20 B F O2	C18 H25 B O3
Formula weight	274.13	300.19
Temperature	130(2) K	130(2) K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	Orthorhombic	Orthorhombic
Space group	P 21 21 21	P 21 21 21
Unit cell dimensions	a = 8.5320(7) Å	a = 6.2351(5) Å
	b = 11.8108(8)Å	b = 12.5482(9) Å
	c = 14.1961(10) Å	c = 20.8610(15) Å
	α = 90°.	α = 90°.
	β = 90°.	β = 90°.
	γ = 90°.	γ = 90°.
Volume	1430.54(18) $Å^3$	1632.1(2) $Å^3$
Z	4	4
Density (calculated)	1.273 g/cm^3	1.222 g/cm^3
Absorption coefficient	0.089 mm^{-1}	0.080 mm^{-1}
F(000)	584	648
Crystal size (mm^3)	0.416 x 0.101 x 0.058	0.460 x 0.240 x 0.150
Theta range for data collection	3.734 to 29.436°.	3.391 to 28.978°.
Index ranges	-11<=h<=11, -14<=k<=15,	-8<=h<=8, -12<=k<=16,
	-18<=l<=17	-23<=l<=26
Reflections collected	15932	5496
Independent reflections	3584 [R(int) = 0.0482]	3498 [R(int) = 0.0330]
Completeness to theta = 25.242°	99.5 %	99.7 %
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	3584 / 0 / 195	3498 / 0 / 205
Goodness-of-fit on F^2	1.044	1.059
Final R indices [I>2sigma(I)]	R1 = 0.0448, wR2 = 0.0896	R1 = 0.0509, wR2 = 0.1013
R indices (all data)	R1 = 0.0625, wR2 = 0.0994	R1 = 0.0730, wR2 = 0.1159
Largest diff. peak and hole	0.205 and -0.207 e.$Å^{-3}$	0.251 and -0.245 e.$Å^{-3}$

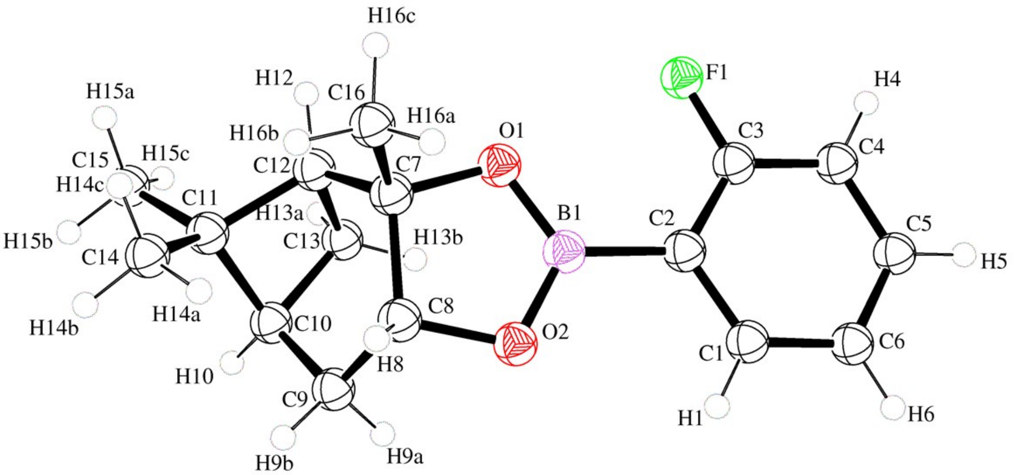


Figure S15. View of the ORTEP plot for boronate ester **2** with labeled atoms. Non-H atoms are represented by 50% probability ellipsoids and H atoms are shown as small circles of arbitrary size.

(1*R*,2*R*,3*S*,5*R*)-(−)-Pinanediol (8.5 mg, 0.05 mmol) in 10 mL of acetonitrile was added to a solution of 2-fluorophenylboronic acid (7.0 mg, 0.05 mmol) in 15 mL of water, the mixture was stirred about 1 h at room temperature. After one day colorless crystals were formed, which were suitable for X-ray crystallography.

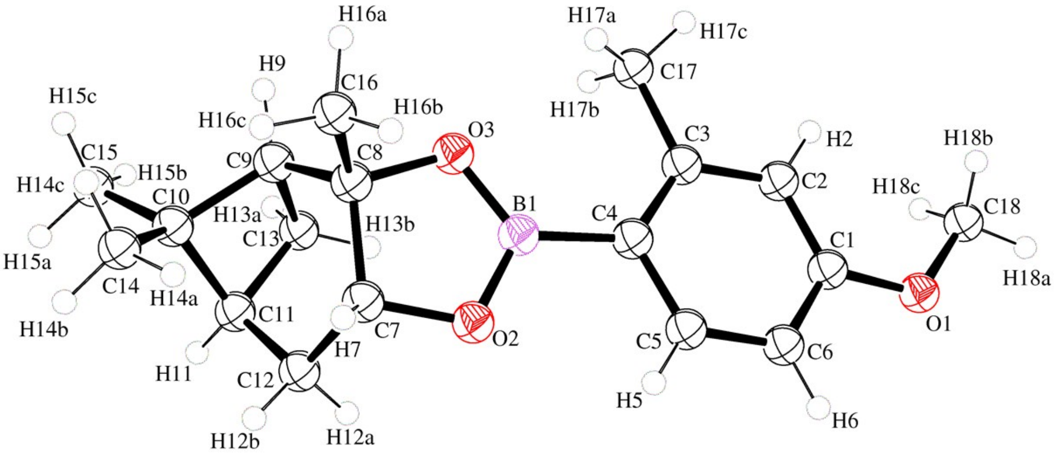


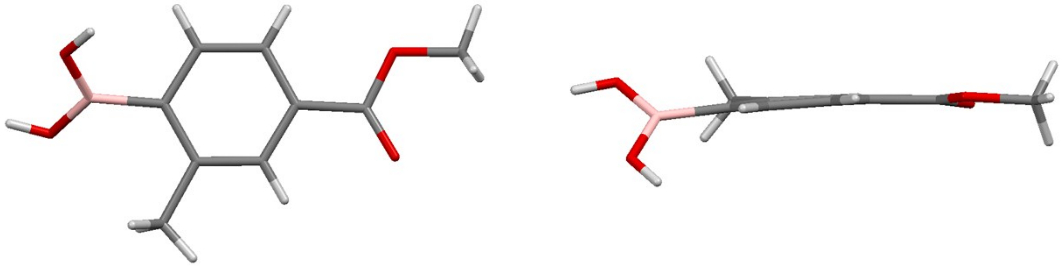
Figure S16. View of the ORTEP plot for boronate ester **3** with labeled atoms. Non-H atoms are represented by 50% probability ellipsoids and H atoms are shown as small circles of arbitrary size.

(1*R*,2*R*,3*S*,5*R*)-(−)-Pinanediol (8.5 mg, 0.05 mmol) in 10 mL of acetonitrile was added to a solution of 4-methoxy-2-methylphenylboronic acid (8.3 mg, 0.05 mmol) in 15 mL of water, the mixture was stirred about 1 h at room temperature. After one day colorless crystals were formed, which were suitable for X-ray crystallography.

Crystal structure determination

All measurements were made on a Oxford Diffraction Gemini "A" diffractometer with a CCD area detector ($\lambda_{\mathrm{MoK}\alpha} = 0.71073$ Å, monochromator: graphite) source equipped with a sealed tube X-ray source. Unit cell constants were determined with a set of 15/3 narrow frame/runs (1° in ω) scans. A data sets consisted of 168/4 frames/runs of intensity data collected with a frame width of 1° in ω, and a crystal-to-detector distance of 55.00 mm. The double pass method of scanning was used to exclude any noise. The collected frames were integrated by using an orientation matrix determined from the narrow frame scans.

Structure solution and refinement were carried out with the SHELXS-2014 and SHELXL-2014 packages;[3] WinGX v2014.1 software was used to prepare material for publication.[4] Full-matrix least-squares refinement was carried out by minimising $(Fo^2 - Fc^2)^2$. All non-hydrogen atoms were refined anisotropically.


top view

side view

Fig. S17. Structure of 2-methyl-4-methoxycarbonylphenylboronic [Stein, T.; Hemme, M.; Hoffmann, F.; Fröba, M. CCDC 1944166: Experimental Crystal Structure Determination, 2019, DOI: 10.5517/ccdc.csd.cc23821j; deposited on 30/07/2019]

Table S2. Absolute energies and the number of imaginary frequencies for calculated structures.

Complex	**Energy (RB+HF-LYP), A.U.**	**Number of imaginary frequencies**
Tetrahedral complex **4**	-972.957984209	0
Chromotropic acid trigonal ester **5**	-791.787635022	0
Chromotropic acid tetrahedral complex **6**	-867.761363817	0

Table S3. Cartesian coordinates.

Tetrahedral complex **4**:
42
symmetry c1

B	5.178591000	5.213754000	5.669937000
C	5.106153000	7.701583000	6.659088000
H	4.574548000	7.965383000	5.751510000
C	5.518381000	6.366299000	6.804963000
C	6.190975000	6.107138000	7.992512000
C	6.459397000	7.032314000	8.989934000
H	6.990521000	6.728812000	9.884581000
C	6.026566000	8.346048000	8.800595000
H	6.220653000	9.093509000	9.561572000
C	5.349319000	8.679750000	7.626933000
H	5.010715000	9.698324000	7.468175000
C	3.068754000	4.140368000	5.271386000
C	3.295796000	5.276448000	4.197017000
H	3.314915000	4.810831000	3.203558000
C	2.210953000	6.402729000	4.182199000
H	2.715367000	7.341829000	4.424983000
H	1.805057000	6.512852000	3.170974000
C	1.070236000	6.172675000	5.181324000
H	0.335986000	6.984309000	5.143967000
C	0.518120000	4.712875000	5.078865000
C	1.731634000	4.334785000	6.011518000
H	1.571675000	3.513550000	6.718138000
C	1.686562000	5.789892000	6.551875000
H	1.000577000	5.920133000	7.388792000
H	2.647984000	6.235890000	6.805831000
C	0.342473000	4.104888000	3.684873000
H	1.227100000	4.185149000	3.055192000
H	-0.475597000	4.617067000	3.166062000
H	0.075666000	3.045374000	3.752707000
C	-0.814572000	4.544896000	5.827216000
H	-1.068710000	3.482881000	5.910973000
H	-1.623214000	5.040230000	5.279031000
H	-0.794875000	4.960141000	6.836234000
C	3.185720000	2.736594000	4.661535000
H	4.143683000	2.639619000	4.144492000
H	2.385642000	2.513283000	3.954583000
H	3.153305000	1.992659000	5.462941000
O	4.130675000	4.305443000	6.203846000
O	4.583218000	5.805881000	4.461571000
F	6.647761000	4.816200000	8.220884000

O	6.422066000	4.497462000	5.270205000
H	6.892025000	4.211251000	6.058530000

Chromotropic acid trigonal ester **5**
30
E(RB+HF-LYP) = -791.787635022 A.U.

C	1.254634000	-3.925691000	0.000000000
C	1.227585000	-1.126628000	0.000000000
C	2.429052000	-1.791570000	0.000000000
C	2.428895000	-3.206360000	0.000000000
H	1.274382000	-5.009493000	0.000000000
H	3.355975000	-1.231751000	0.000000000
H	3.379313000	-3.727475000	0.000000000
C	0.000390000	-1.832120000	0.000000000
C	0.000654000	-3.257840000	0.000000000
C	-1.253145000	-3.926136000	0.000000000
C	-2.427591000	-3.207187000	0.000000000
C	-2.428297000	-1.792351000	0.000000000
C	-1.227105000	-1.127011000	0.000000000
H	-1.272482000	-5.009943000	0.000000000
H	-3.377843000	-3.728617000	0.000000000
H	-3.355473000	-1.232964000	0.000000000
O	-1.198264000	0.250489000	0.000000000
O	1.198331000	0.250872000	0.000000000
B	0.000000000	0.934262000	0.000000000
C	-0.001219000	5.299086000	0.000000000
C	-1.209636000	4.600311000	0.000000000
C	-1.206941000	3.207336000	0.000000000
C	-0.000427000	2.485042000	0.000000000
C	1.205647000	3.208003000	0.000000000
C	1.207577000	4.601002000	0.000000000
H	-0.001532000	6.383528000	0.000000000
H	-2.149197000	5.141483000	0.000000000
H	-2.149267000	2.670904000	0.000000000
H	2.148302000	2.672135000	0.000000000
H	2.146841000	5.142687000	0.000000000

Chromotropic acid tetrahedral complex **6**
32
E(RB+HF-LYP) = -867.761363817 A.U.

O	-1.674740000	-0.000525000	2.730757000
H	-1.048069000	-0.000929000	3.462770000
C	3.236177000	-1.248161000	-1.120209000
C	0.988132000	-1.234233000	0.596434000
C	1.570572000	-2.431213000	0.204255000

C	2.688911000	-2.425680000	-0.655417000
H	4.098262000	-1.260451000	-1.778347000
H	1.150454000	-3.364615000	0.561580000
H	3.122493000	-3.374364000	-0.955344000
C	1.541795000	-0.000025000	0.136048000
C	2.684394000	0.000119000	-0.723178000
C	3.236119000	1.248536000	-1.119869000
C	2.688795000	2.425902000	-0.654761000
C	1.570470000	2.431144000	0.204939000
C	0.988112000	1.234030000	0.596814000
H	4.098199000	1.261039000	-1.778010000
H	3.122317000	3.374691000	-0.954442000
H	1.150330000	3.364431000	0.562540000
O	-0.067720000	1.224842000	1.424265000
O	-0.067767000	-1.225343000	1.423786000
B	-0.956860000	-0.000259000	1.471458000
C	-3.921729000	0.000329000	-1.872262000
C	-3.446333000	1.204531000	-1.350450000
C	-2.506501000	1.196207000	-0.316880000
C	-2.012043000	0.000011000	0.229788000
C	-2.506789000	-1.196031000	-0.316994000
C	-3.446620000	-1.204038000	-1.350568000
H	-4.650058000	0.000461000	-2.676454000
H	-3.806304000	2.147462000	-1.750561000
H	-2.142481000	2.142716000	0.071680000
H	-2.142989000	-2.142656000	0.071479000
H	-3.806812000	-2.146845000	-1.750775000