# Origins of the Relative Stabilities of Anhydrous and Hydrated D-Mannitol Crystals

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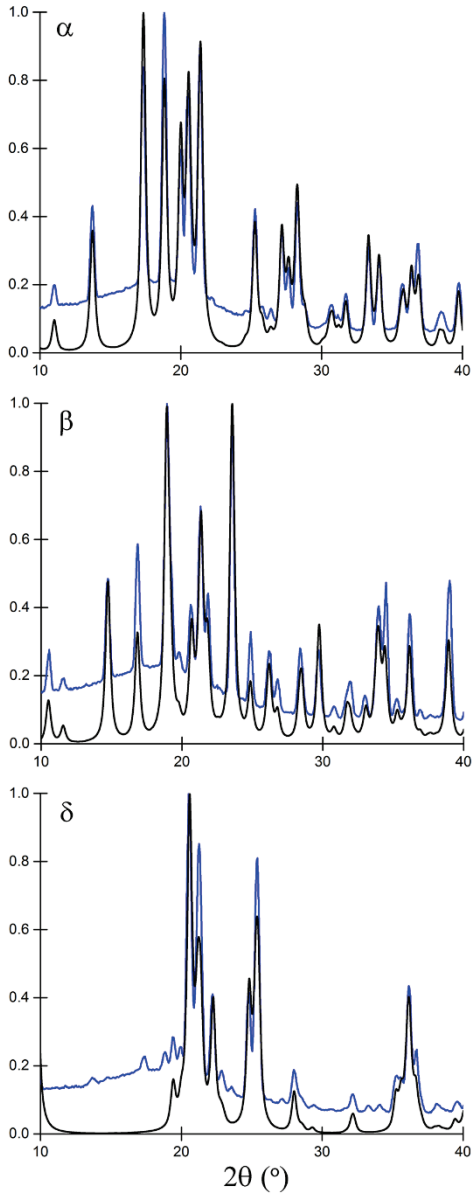


**Figure S1.** Experimental PXRD data (blue) for α, β, and δ mannitol compared to X-ray data published in Fronczek, F.; Kamel, H. N.; Slattery, M. *Acta Crystallogr., Sect. C*. **2003,** *59*, 567-570 (black).

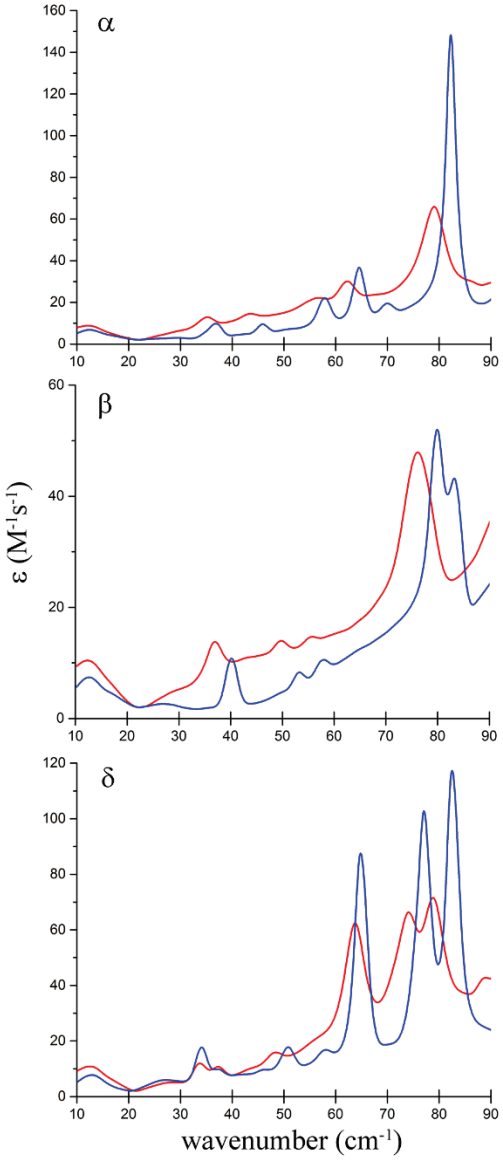


**Figure S2.** Terahertz spectra collected at 293 K (red) and 78 K (blue) from 10 to 90 $cm^{-1}$ for the anhydrous polymorphs.

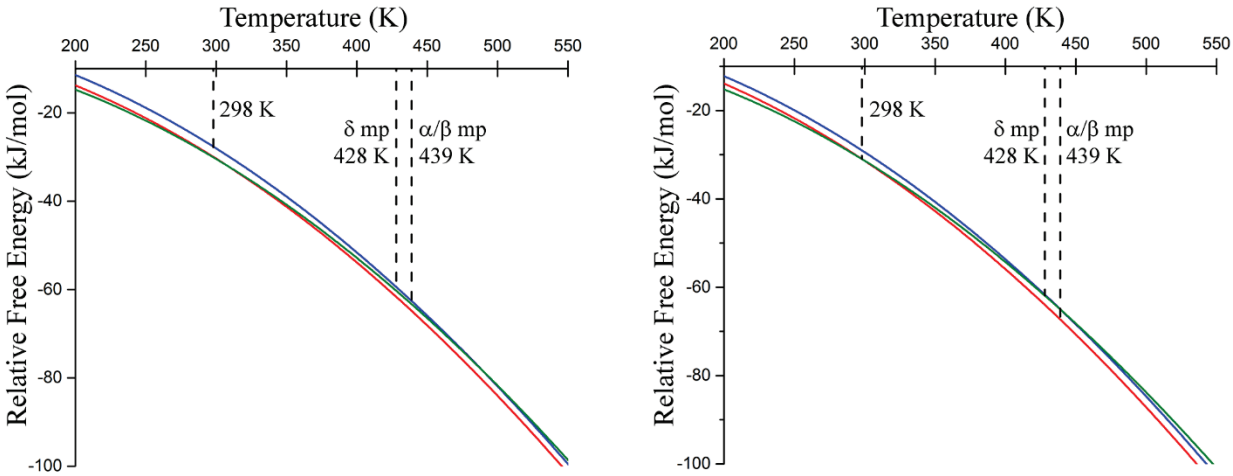


**Figure S3.** Gibbs free energy data calculated for each anhydrous mannitol polymorph over the temperature range of 0.0 – 600.0 K. The relative free energy for the fully optimized (left) and constant-volume optimized (right) structures of the α (blue), β (red), and δ (green) polymorphs was plotted over the range of 200.0 K – 550.0 to more clearly show the enantiotropic transitions.

**Table S1.** Comparison of optimized structures simulated with 6-311G(d,p) and Ahlrich's VTZ with polarization functions (VTZP).

| | α | | | β | | | δ | | |
|---|---|---|---|---|---|---|---|---|---|
| | **6-311G(d,p)** | | | | | | | | |
| | **Exp.** | **Calc.** | **% Err** | **Exp.** | **Calc.** | **% Err** | **Exp.** | **Calc.** | **% Err** |
| ***a*** | 4.8653 | 4.8280 | -0.77 | 5.5381 | 5.4998 | -0.69 | 4.899 | 4.855 | -0.90 |
| ***b*** | 8.873 | 8.671 | -2.27 | 8.580 | 8.369 | -2.46 | 18.268 | 18.109 | -0.87 |
| ***c*** | 18.739 | 18.454 | -1.52 | 16.795 | 16.392 | -2.39 | 5.043 | 4.978 | -1.29 |
| ***V*** | 808.959 | 772.572 | -4.50 | 798.046 | 754.478 | -5.46 | 397.043 | 383.509 | -3.41 |
| | **Abs. Avg. %Err** | | 2.26 | **Abs. Avg. %Err** | | 2.75 | **Abs. Avg. %Err** | | 1.62 |
| | | | | | | | | | |
| | **VTZP** | | | | | | | | |
| ***a*** | 4.8653 | 4.8766 | +0.23 | 5.5381 | 5.5230 | -0.27 | 4.899 | 4.870 | -0.59 |
| ***b*** | 8.873 | 8.678 | -2.19 | 8.580 | 8.411 | -1.97 | 18.268 | 18.148 | -0.65 |
| ***c*** | 18.739 | 18.556 | -0.97 | 16.795 | 16.547 | -1.48 | 5.043 | 4.999 | -0.86 |
| ***V*** | 808.959 | 785.321 | -2.92 | 798.046 | 768.681 | -3.68 | 397.043 | 387.617 | -2.37 |
| | **Abs. Avg. %Err** | | 1.58 | **Abs. Avg. %Err** | | 1.85 | **Abs. Avg. %Err** | | 1.12 |

**Table S2.** Comparisons of BSSE in kJ/mol calculated with 6-311G(d,p) and VTZP for the anhydrous mannitol polymorphs.

| | **6-311G(d,p)** | **Ahlrich's pVTZ** |
|---|---|---|
| **α** | 69.17 | 19.43 |
| **β** | 72.75 | 19.73 |
| **δ** | 76.34 | 23.24 |

**Table S3.** Frequencies ($cm^{-1}$) of terahertz spectral peaks for the anhydrous polymorphs and their temperature correlations.

| α | | β | | δ | |
|---|---|---|---|---|---|
| **293 K** | **78 K** | **293 K** | **78 K** | **293 K** | **78 K** |
| 35.4 | 36.4 | 36.4 | 40.1 | 33.7 | 34.0 |
| 43.7 | 45.8 | 50.0 | 53.1 | 37.5 | 38.0 |
| 57.3 | 58.3 | 56.2 | 58.3 | 47.9 | 50.7 |
| 62.5 | 64.5 | 76.0 | 79.8 | | 56.7 |
| | 69.8 | | 83.4 | 63.6 | 64.9 |
| 79.1 | 82.3 | | | 73.6 | 77.0 |
| | | | | 79.1 | 82.7 |

**Table S4**. Lattice parameters and fractional coordinates of the refined hemihydrate structure

| | | | |
|---|---|---|---|
| a | 9.607991 | α | 102.9253 |
| b | 10.13037 | β | 89.4453 |
| c | 4.747702 | γ | 112.742 |
| V | 413.8625 | | |
| | | | |

| | X/A | Y/B | Z/C | | X/A | Y/B | Z/C |
|---|---|---|---|---|---|---|---|
| C | -0.44558 | 0.217386 | 0.13636 | O | 0.338103 | -0.45453 | -0.29474 |
| C | -0.31407 | 0.348365 | 0.319701 | O | 0.369597 | -0.29881 | 0.247486 |
| C | -0.36693 | 0.47057 | 0.46178 | O | 0.143144 | -0.22581 | -0.16281 |
| C | -0.23502 | -0.38492 | -0.39769 | O | 0.196049 | -0.06183 | 0.365274 |
| C | -0.28827 | -0.26002 | -0.27806 | H | 0.220897 | 0.249483 | -0.49923 |
| C | -0.16146 | -0.12118 | -0.10245 | H | 0.100433 | 0.160563 | 0.175397 |
| O | -0.40825 | 0.09227 | 0.028307 | H | 0.286181 | 0.410009 | 0.166104 |
| O | -0.18915 | 0.399062 | 0.152353 | H | 0.112706 | -0.48955 | -0.35088 |
| O | -0.46691 | 0.414952 | -0.33009 | H | 0.146628 | -0.3459 | 0.284414 |
| O | -0.15672 | -0.40904 | -0.17144 | H | 0.37265 | -0.17488 | -0.18418 |
| O | -0.35149 | -0.23451 | 0.476746 | H | 0.414448 | -0.02526 | 0.470579 |
| O | -0.02562 | -0.07366 | -0.24691 | H | 0.322243 | 0.037721 | -0.23807 |
| H | -0.47537 | 0.249416 | -0.05164 | H | 0.110357 | -0.04949 | 0.460858 |
| H | 0.4568 | 0.187255 | 0.264787 | H | 0.172159 | -0.16705 | 0.04047 |
| H | -0.27238 | 0.31434 | 0.492194 | H | 0.461971 | -0.28899 | 0.355622 |
| H | -0.42643 | 0.493231 | 0.294559 | H | 0.339286 | -0.39893 | -0.09511 |
| H | -0.15859 | -0.35167 | 0.436194 | H | -0.02223 | 0.384097 | 0.139709 |
| H | -0.37625 | -0.29528 | -0.13098 | H | 0.029113 | 0.283438 | -0.27319 |
| H | -0.13798 | -0.1418 | 0.10453 | O | -0.29158 | 0.04947 | -0.49024 |
| H | -0.19912 | -0.03063 | -0.05561 | H | -0.18275 | 0.110807 | -0.49002 |
| H | 0.02997 | -0.13252 | -0.21508 | H | -0.32389 | 0.079546 | -0.29701 |
| H | -0.31876 | -0.12799 | 0.492125 | O | 0.338103 | -0.45453 | -0.29474 |
| H | -0.04821 | -0.36242 | -0.18474 | O | 0.369597 | -0.29881 | 0.247486 |
| H | 0.457101 | 0.457794 | -0.31626 | O | 0.143144 | -0.22581 | -0.16281 |
| H | -0.20499 | 0.455814 | 0.022228 | O | 0.196049 | -0.06183 | 0.365274 |
| H | -0.37206 | 0.068332 | 0.195066 | H | 0.220897 | 0.249483 | -0.49923 |
| C | 0.129383 | 0.251194 | 0.368456 | | | | |
| C | 0.181709 | 0.395876 | 0.272662 | | | | |
| C | 0.212412 | -0.46942 | -0.47379 | | | | |
| C | 0.245015 | -0.32845 | 0.422805 | | | | |
| C | 0.274531 | -0.1936 | -0.32599 | | | | |
| C | 0.308895 | -0.05196 | -0.4259 | | | | |
| O | -0.00258 | 0.228923 | -0.47706 | | | | |
| O | 0.074765 | 0.390104 | 0.060311 | | | | |

**Table S5.** Simulated frequencies and intensities of the refined hemihydrate structure.

| Frequency ($cm^{-1}$) | Intensity (km/mol) | Frequency ($cm^{-1}$) | Intensity (km/mol) | Frequency ($cm^{-1}$) | Intensity (km/mol) | Frequency ($cm^{-1}$) | Intensity (km/mol) |
|---|---|---|---|---|---|---|---|
| 51.8614 | 4.0273 | 443.2881 | 30.3213 | 1044.84 | 299.7898 | 1416.459 | 9.9308 |
| 56.8677 | 14.1352 | 461.0101 | 12.4384 | 1048.523 | 144.5092 | 1421.754 | 12.7377 |
| 68.6305 | 2.167 | 497.9258 | 23.0986 | 1057.95 | 389.7714 | 1429.465 | 19.683 |
| 87.5031 | 1.894 | 510.6677 | 35.2258 | 1066.037 | 60.9327 | 1429.707 | 46.7466 |
| 93.3217 | 3.0161 | 519.0083 | 50.8981 | 1070.843 | 114.3136 | 1436.588 | 47.7363 |
| 95.5676 | 0.8755 | 536.8444 | 52.647 | 1080.659 | 15.8618 | 1442.095 | 114.4263 |
| 107.8393 | 17.1237 | 538.1302 | 21.0818 | 1091.168 | 52.2679 | 1459.706 | 30.1819 |
| 110.4593 | 6.7689 | 555.0263 | 203.6651 | 1105.128 | 275.3716 | 1462.125 | 64.1875 |
| 133.5553 | 4.1885 | 598.4601 | 21.9117 | 1105.483 | 42.9562 | 1471.201 | 106.7044 |
| 143.3082 | 2.7867 | 646.1733 | 101.4937 | 1112.269 | 139.0108 | 1482.728 | 62.6982 |
| 154.8386 | 3.6694 | 651.2752 | 13.598 | 1120.896 | 53.4826 | 1488.837 | 182.4178 |
| 157.1949 | 8.9526 | 661.7494 | 12.6752 | 1134.783 | 114.4788 | 1491.224 | 19.7957 |
| 164.2936 | 9.3874 | 679.8548 | 14.6892 | 1135.503 | 20.6379 | 1507.458 | 1.7919 |
| 174.837 | 9.8578 | 710.6007 | 376.1607 | 1144.74 | 49.9399 | 1509.352 | 59.5136 |
| 190.4225 | 14.7718 | 721.4863 | 8.2405 | 1156.625 | 18.8904 | 1514.167 | 18.0531 |
| 204.1443 | 6.5782 | 751.9393 | 204.7881 | 1168.783 | 33.916 | 1525.863 | 107.0552 |
| 210.5449 | 36.3556 | 766.4041 | 99.4415 | 1169.6 | 22.6896 | 1527.728 | 31.597 |
| 218.357 | 10.9963 | 787.4164 | 19.8823 | 1240.093 | 29.3814 | 1535.156 | 21.9072 |
| 221.7064 | 27.8254 | 793.6438 | 5.4274 | 1253.156 | 29.7612 | 1554.605 | 138.2918 |
| 233.0581 | 0.3877 | 805.5188 | 66.0798 | 1264.264 | 20.6572 | 1574.518 | 112.7211 |
| 244.877 | 17.5505 | 819.8585 | 95.0985 | 1272.04 | 33.0031 | 1700.761 | 49.5835 |
| 253.3694 | 1.5909 | 839.5372 | 181.2985 | 1282.604 | 43.4063 | 3055.375 | 35.8852 |
| 259.4349 | 3.4417 | 848.0495 | 363.1264 | 1292.194 | 3.5925 | 3060.9 | 68.9259 |
| 272.2811 | 23.455 | 858.8875 | 263.1604 | 1303.79 | 83.4494 | 3066.973 | 62.2002 |
| 281.2087 | 2.5255 | 883.1215 | 115.7319 | 1311.806 | 47.8918 | 3067.853 | 32.9718 |
| 285.9259 | 9.4132 | 883.8534 | 67.44 | 1324.983 | 13.2031 | 3078.588 | 45.8707 |
| 297.4335 | 6.0678 | 900.6123 | 32.7242 | 1336.919 | 29.1824 | 3086.085 | 59.765 |
| 305.4809 | 29.4305 | 905.6623 | 51.3647 | 1353.353 | 28.1532 | 3090.916 | 1.0359 |
| 315.1186 | 21.6872 | 907.5639 | 172.0276 | 1357.096 | 22.471 | 3104.59 | 36.6713 |
| 318.8662 | 4.5683 | 910.2369 | 30.4895 | 1359.384 | 55.9908 | 3108.34 | 29.8047 |
| 330.9939 | 9.0025 | 921.7348 | 365.9481 | 1372.276 | 70.1161 | 3110.422 | 71.473 |
| 346.1055 | 26.3952 | 946.1268 | 31.0256 | 1375.319 | 69.8491 | 3116.963 | 33.0441 |
| 350.3618 | 22.1723 | 959.6773 | 154.6588 | 1380.111 | 56.1862 | 3117.851 | 9.1713 |
| 359.016 | 43.9748 | 968.0354 | 39.7477 | 1391.906 | 6.8571 | 3128.639 | 33.8222 |
| 375.0239 | 4.9137 | 982.1921 | 107.041 | 1393.509 | 7.6416 | 3130.64 | 49.5974 |
| 376.5504 | 47.093 | 992.3467 | 72.3904 | 1404.338 | 22.248 | 3141.482 | 130.8691 |
| 435.8809 | 16.9778 | 1022.17 | 293.6652 | 1407.54 | 12.0906 | 3164.291 | 14.7931 |

| Frequency ($cm^{-1}$) | Intensity (km/mol) |
|---|---|
| 3234.649 | 2168.893 |
| 3273.551 | 3829.841 |
| 3315.059 | 304.1689 |
| 3337.677 | 29.6561 |
| 3367.604 | 3088.877 |
| 3384.464 | 1469.144 |
| 3409.532 | 4102.245 |
| 3417.152 | 471.3177 |
| 3493.629 | 1246.916 |
| 3536.914 | 1401.42 |
| 3539.765 | 147.2816 |
| 3558.501 | 342.3875 |
| 3633.445 | 573.6256 |
| 3671.295 | 1217.803 |