CRYSTAL STRUCTURES OF LARGE-VOLUME COMMERCIAL PHARMACEUTICALS

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As part of a continuing project, the challenging room-temperature crystal structures of four commercial pharmaceutical APIs have been solved by Monte Carlo simulated annealing techniques using synchrotron X-ray powder diffraction data (11-BM at APS), and optimized using density functional techniques. **Bisoprolol fumarate**, $(C_{18}H_{33}NO_4)_2(C_4H_2O_4)$, crystallizes in $P\bar{1}$, with a = 8.16570(5), b = 8.51639(12), c = 16.75179(18) Å, α = 89.142(1), β = 78.155(1), γ = 81.763(1)°, V = 1128.265(10) Å^3, and Z = 1. The structure was difficult to solve because the two ends of the bisoprolol cation are similar but not identical. **Hyoscyamine sulfate monohydrate**, $(C_{17}H_{24}NO_3)_2(SO_4)(H_2O)$, (generally described as a dihydrate) crystallizes in $P2_1$ with a = 6.60196(2), b = 12.95496(3), c = 20.93090(8) Å, β = 94.8839(2)°, V = 1783.680(5) Å^3, and Z = 2. The multiple fragments led to a low success rate. **Atropine sulfate monohydrate**, $(C_{17}H_{24}NO_3)_2(SO_4)(H_2O)$, (racemic hyoscyamine) crystallizes in $P2_1/n$ with a = 19.2948(5), b = 6.9749(2), c = 26.9036(5) Å, β = 94.215(2)°, V = 3610.86(9) Å^3, and Z = 4. The success rate of solution using DASH was only 1%, and required Mogul Distribution Bias and {010} preferred orientation. Despite being apparently orthorhombic **cefprozil monohydrate**, $C_{18}H_{19}N_3O_5S(H_2O)$, crystallizes in $P2_1$ with a = 11.26503(5), b = 11.34017(4), c = 14.72628(10) Å, β = 90.1249(4)°, V = 1881.24(2) Å^3, and Z = 4. DFT calculations suggest that the carboxylic acid proton on one (but not the other) of the two independent cefprozil molecules is transferred to an amino group, forming a salt. This suggestion needs to be confirmed by spectroscopic experiments and calculations of the vibrational spectrum. Hydrogen bonding is important in all these crystal structures.