

Electronic Supplementary Information

Solubility Improvement of Epalrestat by Layered Structure Formation via Cocrystallization

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Table S1. Hydrogen bond for EPR-DMF solvate

| D-H...A | D-H (Å) | H...A (Å) | D...A (Å) | D-H...A (°) |
|---------------------------|---------|-----------|------------|-------------|
| C17-H17B...O1 | 0.98 | 2.51 | 3.239(2) | 130.8 |
| C3-H3...S1 ¹ | 0.95 | 2.85 | 3.6609(18) | 144.3 |
| C16-H16B...O1 | 0.98 | 2.51 | 3.195(2) | 127.0 |
| O3-H3A...O4 ² | 0.91(3) | 1.63(3) | 2.5392(18) | 177(3) |
| C9-H9B...S1 | 0.98 | 2.60 | 3.2179(18) | 121.4 |
| C10-H10...O1 | 0.99(2) | 2.509(18) | 2.888(2) | 102.3(12) |
| C14-H14A...S2 | 0.99 | 2.74 | 3.1269(18) | 103.6 |
| C16-H16C...O4 | 0.98 | 2.36 | 2.771(2) | 104.5 |
| C18-H18...O2 ³ | 0.98(2) | 2.54(2) | 3.493(2) | 165.5(2) |
| C18-H18...O3 ³ | 0.98(2) | 2.56(3) | 3.379(3) | 141.7(2) |

¹x-1,y-1,z; ²-x+2,-y+2,-z+1; ³x,-1+y,z

Table S2. Hydrogen bond for EPR-DMSO solvate

| D-H...A | D-H (Å) | H...A (Å) | D...A (Å) | D-H...A (°) |
|----------------------------|---------|-----------|-----------|-------------|
| C14-H14B...O5 ¹ | 0.99 | 2.33 | 3.185(3) | 144.5 |
| C1-H1...O2 ² | 0.95 | 2.44 | 3.237(4) | 140.8 |
| O3-H3A...O4 ³ | 0.87(4) | 1.72(4) | 2.572(3) | 167(4) |
| O3-H3A...S3 ³ | 0.87(4) | 2.86(4) | 3.698(3) | 164(3) |
| C19-H19C...O3 ⁴ | 0.98 | 2.57 | 3.396(4) | 141.4 |
| C18-H18B...O4 | 0.98 | 2.43 | 3.396(4) | 167.4 |
| C17-H17B...O5 ¹ | 0.98 | 2.60 | 3.410(4) | 140.6 |
| C16-H16C...O2 | 0.98 | 2.59 | 3.513(4) | 157.2 |
| C2-H2...O5 ⁵ | 0.95 | 2.51 | 3.407(4) | 157.0 |
| C3-H3...O1 ⁶ | 0.95 | 2.59 | 3.313(3) | 132.9 |
| C9-H9B...S1 | 0.98 | 2.63 | 3.165(3) | 114.8 |
| C10-H10...O1 | 0.98(3) | 2.50(3) | 2.891(4) | 103.3(17) |
| C14-H14B...O1 | 0.99 | 2.48 | 2.838(3) | 100.6 |

¹x-1,y-1,z; ²-x+1,-y+2,-z+1;³-x,-y+1,-z; ⁴x+1,y+1,z;⁵-x+2,-y+2,-z+1;

⁶-x+1,-y+1,-z+1

List of the unsuccessful cofomers used in this study

- Recorcinol
- Pyrogallol
- Benzoic acid
- 2-hydroxy benzoic acid
- 3-hydroxy benzoic acid
- Nicotinamide
- Isonicotinamide
- Benzamide
- Oxalic acid
- Fumaric acid
- Nicotinic acid
- Isonicotinic acid
- Oxalic acid
- Malonic acid
- Succinic acid
- Glutaric acid
- Adipic acid
- Pimelic acid
- Theophylline
- 8-chlorotheophylline
- Proline
- Glycine
- Arginine
- 2,2'-bipyridine
- 2,3'-bipyridine
- 2,4'-bipyridine
- 3,3'-bipyridine
- 3,4'-bipyridine
- 4,4'-bipyridine