

# Supplementary Materials: Structural Polymorphism of Sorafenib Tosylate as a Key Factor in Its Solubility Differentiation

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**Table S1.** Selected characteristic vibronic features of sorafenib tosylate in theory with application of 6-31G(d,p) basis and experiment bands of sorafenib tosylate (def.-deformation, s-stretching, b-bending, oop out of the plane).

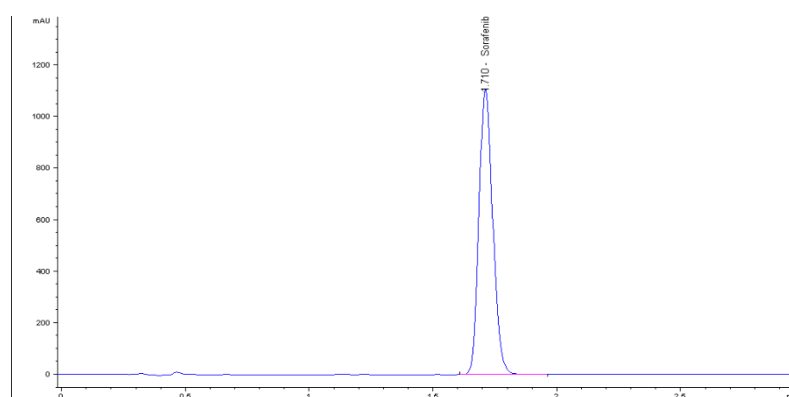
| $V_{exp.R}$ |       | $V_{exp.IR}$ |       | $\nu_t$ | Bands assignment                                                                   |
|-------------|-------|--------------|-------|---------|------------------------------------------------------------------------------------|
| S I         | S III | S I          | S III |         |                                                                                    |
|             | 509   | 512          | 508   | 535     | C-H def. oop in methylobenzene sulfonate ring                                      |
|             |       | 567          | 571   | 550     | Def. methylobenzene sulfonate ring                                                 |
| 662         | 664   | 661          | 664   | 657     | C-S s + def. methylobenzene sulfonate ring                                         |
| 684         | 683   | 681          | 681   | 671     | Def. 4-chloro-3trifluoromethylphenyl ring                                          |
|             |       | 711          | 711   | 687     | N(1)-H def. oop in ureido                                                          |
| 719         | 717   | 720          | 722   | 706     | N(4)-H def. oop in in methylamide                                                  |
|             | 817   | 820          | 818   | 825     | C-H def. oop                                                                       |
|             |       | 846          | 846   | 846     | C-H def. oop                                                                       |
|             |       | 877          | 879   | 873     | S-O s in methylobenzene sulfonate                                                  |
| 921         | 928   | 920          | 922   | 920     | C-H def. oop                                                                       |
|             |       | 950          | 948   | 950     | Def. 4-chloro-3trifluoromethylphenyl, phenoxy and pyridine-2-carboxylic acid rings |
| 1010        | 1009  | 1010         | 1010  | 1017    | C-C s + C-N s in pyridine-2-carboxylic acid                                        |
| 1030        | 1035  | 1032         | 1034  | 1038    | C-C s + C-Cl s in 4-chloro-3trifluoromethylphenyl                                  |
| 921         | 928   | 920          | 922   | 920     | C-H def. oop                                                                       |
|             |       | 950          | 948   | 950     | Def. 4-chloro-3trifluoromethylphenyl, phenoxy and pyridine-2-carboxylic acid rings |
| 1010        | 1009  | 1010         | 1010  | 1017    | C-C s + C-N s in pyridine-2-carboxylic acid                                        |
| 1030        | 1035  | 1032         | 1034  | 1038    | C-C s + C-Cl s in 4-chloro-3trifluoromethylphenyl                                  |
| 1115        | 1118  | 1117         | 1119  | 1143    | C-S s + S=O s in methylobenzene sulfonate                                          |
| 1164        | 1161  | 1184         | 1177  | 1193    | C-F s in 4-chloro-3trifluoromethylphenyl                                           |

|      |      |      |      |      |                                                                                                                                                   |
|------|------|------|------|------|---------------------------------------------------------------------------------------------------------------------------------------------------|
|      |      | 950  | 948  | 950  | Def. 4-chloro-3trifluoro-methylphenyl, phenoxy and pyridine-2-carboxylic acid rings                                                               |
| 1010 | 1009 | 1010 | 1010 | 1017 | C-C s + C-N s in pyridine-2-carboxylic acid                                                                                                       |
| 1030 | 1035 | 1032 | 1034 | 1038 | C-C s + C-Cl s in 4-chloro-3trifluoromethylphenyl                                                                                                 |
| 1115 | 1118 | 1117 | 1119 | 1143 | C-S s + S=O s in methylbenzene sulfonate                                                                                                          |
| 1164 | 1161 | 1184 | 1177 | 1193 | C-F s in 4-chloro-3trifluoro-methylphenyl                                                                                                         |
| 1186 | 1182 | 1190 | 1188 | 1217 | C-F s + C-H b in 4-chloro-3trifluoromethylphenyl and methylbenzene sulfonate                                                                      |
|      | 1215 | 1218 | 1208 | 1230 | C-O(2) s in pyridine-2-carboxylic acid + C-C s + C-H def. in phenoxy ring                                                                         |
| 1241 | 1238 | 1238 | 1234 | 1266 | C-N(4)-H b in methylamine + C-O(2) s in pyridine-2-carboxylic acid + C-H def. in pyridine-2-carboxylic acid and 4-chloro-3trifluoromethylphenyl , |
| 1268 | 1265 | 1255 | 1260 | 1297 | C-N s + C-N-H b in ureido + C-C s + C-F s in 4-chloro-3trifluoro-methylphenyl ,                                                                   |
|      | 1285 | 1279 | 1283 | 1337 | C-N(3) s + C-H def. in pyridine-2-carboxylic acid                                                                                                 |
| 1310 | 1313 | 1309 | 1309 | 1350 | C-N(2) s C-O s in ureido + C-C s in 4-chloro-3trifluoromethylphenyl , phenoxy and pyridine-2-carboxylic acid                                      |
| 1327 | 1336 | 1327 | 1338 | 1369 | C-N(1) s in ureido + C-C s + C-F s in 4-chloro-3trifluoro-methylphenyl                                                                            |
|      |      | 1419 | 1420 | 1434 | C-N(2)-H def. in ureido + C-C s + C-H def. in phenoxy ring                                                                                        |
|      |      | 1459 | 1461 | 1459 | C-C s + C-N(1) def. + C-F s in in 4-chloro-3trifluoromethylphenyl and ureido                                                                      |
|      |      | 1483 | 1483 | 1521 | C-N(1) s + C-C s + C-H def. in ureido                                                                                                             |
| 1506 | 1505 | 1505 | 1502 | 1549 | C-C s in phenoxy rings + C-H def. in phenoxy ring                                                                                                 |
|      |      | 1528 | 1528 | 1586 | C-N(1)-H b in ureido                                                                                                                              |
|      | 1551 | 1556 | 1550 | 1605 | C-N(4)-H b in methylamide                                                                                                                         |
| 1609 | 1606 | 1597 | 1604 | 1644 | C=C s in 4-chloro-3trifluoro-methylphenyl and in pyridine-2-                                                                                      |

|      |      |      |      |      |                                                                                                                |
|------|------|------|------|------|----------------------------------------------------------------------------------------------------------------|
| 1629 | 1632 | 1629 | 1632 | 1666 | carboxylic acid + C-N-H b in ureido<br>C=C s in 4-chloro-3trifluoromethylphenyl and phenoxy rings + C-N(1)-H b |
| 1688 | 1690 | 1688 | 1691 | 1716 | C=O s in pyridine-2-carboxylic acid                                                                            |
| 1723 | 1715 | 1721 | 1714 | 1792 | C=O s in ureido                                                                                                |

**Table S2.** Parameters of liquid chromatography separation of sorafenib tosylate.

| Parameters                 | Determination of sorafenib tosylate                                     |
|----------------------------|-------------------------------------------------------------------------|
| Stationary phase (column): | Octadecylsilica column (3 $\mu$ m, 50 mm $\times$ 4.6 mm i.d.)          |
| Mobile phase:              | A: 0.02 M of sodium dihydrogen phosphate (35%)<br>B: acetonitrile (65%) |
| Mobile Phase Flow Rate:    | 1.5 mL/min                                                              |
| Column temperature:        | 313K                                                                    |
| Detection Wavelength:      | 266 nm                                                                  |
| Injection volume:          | 5 $\mu$ L                                                               |

**Figure S1.** Sorafenib tosylate chromatogram.