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**Supporting information**

# Consensus based comparison of chromatographic and computational estimated lipophilicity of benzothiepino[3,2-c]pyridine derivatives as potential antifungal drugs

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**Content**

**Table S1**. Retention parameters ($R_F$) of dibenzo[*b*,*f*]thiepines in typical reversed-phase and microemulsion chromatographic systems.

| Comp. No. | Typical reversed-phase TLC | | | | | | | | | | | | | | | | MELC-TLC | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Organic modifier | | | | | | | | | | | | | | | | | |
| | Acetone | | | | | | Methanol | | | | | Dioxane | | | | | MELC1 | MELC2 |
| | 90% | 85% | 80% | 75% | 70% | 65% | 98% | 94% | 90% | 86% | 82% | 85% | 80% | 75% | 70% | 65% | | |
| **1** | 0.63 | 0.62 | 0.57 | 0.52 | 0.48 | 0.41 | 0.53 | 0.48 | 0.46 | 0.44 | 0.4 | 0.84 | 0.75 | 0.71 | 0.62 | 0.37 | 0.30 | 0.43 |
| **2** | 0.73 | 0.62 | 0.50 | 0.35 | 0.28 | 0.17 | 0.56 | 0.47 | 0.44 | 0.36 | 0.28 | 0.77 | 0.67 | 0.60 | 0.49 | 0.25 | 0.29 | 0.40 |
| **3** | 0.59 | 0.50 | 0.42 | 0.29 | 0.23 | 0.14 | 0.45 | 0.36 | 0.32 | 0.27 | 0.18 | 0.74 | 0.64 | 0.53 | 0.37 | 0.16 | 0.27 | 0.37 |
| **4** | 0.58 | 0.46 | 0.40 | 0.23 | 0.19 | 0.08 | 0.37 | 0.26 | 0.23 | 0.17 | 0.13 | 0.76 | 0.64 | 0.50 | 0.32 | 0.11 | 0.23 | 0.33 |
| **5** | 0.64 | 0.52 | 0.44 | 0.26 | 0.24 | 0.12 | 0.44 | 0.34 | 0.32 | 0.24 | 0.17 | 0.78 | 0.66 | 0.51 | 0.35 | 0.14 | 0.21 | 0.31 |
| **6** | 0.66 | 0.53 | 0.46 | 0.29 | 0.24 | 0.12 | 0.42 | 0.32 | 0.30 | 0.23 | 0.14 | 0.82 | 0.70 | 0.53 | 0.39 | 0.16 | 0.21 | 0.31 |
| **7** | 0.66 | 0.51 | 0.45 | 0.25 | 0.22 | 0.09 | 0.48 | 0.38 | 0.35 | 0.26 | 0.18 | 0.78 | 0.67 | 0.51 | 0.37 | 0.15 | 0.21 | 0.30 |
| **8** | 0.66 | 0.55 | 0.51 | 0.35 | 0.33 | 0.21 | 0.50 | 0.42 | 0.41 | 0.35 | 0.25 | 0.83 | 0.76 | 0.60 | 0.46 | 0.23 | 0.26 | 0.37 |
| **9** | 0.64 | 0.50 | 0.45 | 0.29 | 0.27 | 0.14 | 0.46 | 0.38 | 0.35 | 0.29 | 0.20 | 0.79 | 0.69 | 0.53 | 0.42 | 0.22 | 0.22 | 0.32 |
| **10** | 0.63 | 0.47 | 0.41 | 0.22 | 0.21 | 0.08 | 0.43 | 0.31 | 0.28 | 0.20 | 0.14 | 0.76 | 0.66 | 0.49 | 0.34 | 0.17 | 0.19 | 0.30 |
| **11** | 0.63 | 0.45 | 0.41 | 0.24 | 0.18 | 0.11 | 0.42 | 0.30 | 0.28 | 0.20 | 0.15 | 0.78 | 0.67 | 0.52 | 0.32 | 0.19 | 0.23 | 0.33 |
| **12** | 0.64 | 0.47 | 0.42 | 0.25 | 0.21 | 0.10 | 0.35 | 0.24 | 0.21 | 0.15 | 0.12 | 0.82 | 0.69 | 0.52 | 0.35 | 0.15 | 0.23 | 0.33 |
| **13** | 0.73 | 0.53 | 0.46 | 0.31 | 0.11 | 0.11 | 0.53 | 0.41 | 0.39 | 0.29 | 0.20 | 0.88 | 0.74 | 0.57 | 0.37 | 0.18 | 0.22 | 0.32 |
| **14** | 0.67 | 0.50 | 0.42 | 0.27 | 0.22 | 0.09 | 0.42 | 0.29 | 0.26 | 0.18 | 0.14 | 0.77 | 0.68 | 0.53 | 0.36 | 0.16 | 0.23 | 0.33 |
| **15** | 0.76 | 0.56 | 0.48 | 0.31 | 0.25 | 0.10 | 0.53 | 0.42 | 0.39 | 0.3 | 0.24 | 0.83 | 0.74 | 0.57 | 0.43 | 0.15 | 0.24 | 0.33 |
| **16** | 0.75 | 0.58 | 0.56 | 0.39 | 0.35 | 0.23 | 0.49 | 0.42 | 0.39 | 0.33 | 0.26 | 0.76 | 0.72 | 0.62 | 0.52 | 0.25 | 0.30 | 0.39 |
| **17** | 0.71 | 0.56 | 0.53 | 0.33 | 0.32 | 0.22 | 0.54 | 0.46 | 0.43 | 0.39 | 0.28 | 0.72 | 0.70 | 0.56 | 0.47 | 0.21 | 0.31 | 0.40 |

**Table S2a**. *In silico* estimated log*P* values and solubility parameter of benzothiepino[3,2-c]pyridine derivtaves.

| Comp. No | miLogP | KOWWIN | AlogPs | AClogP | AlogP | MLOGP | XlogP2 | XlogP3 | AlogpS* |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 2.66 | 2.70 | 2.14 | 2.29 | 1.80 | 1.51 | 1.90 | 2.34 | -2.83 |
| **2** | 3.75 | 3.73 | 3.54 | 3.37 | 2.95 | 2.60 | 3.15 | 3.14 | -4.05 |
| **3** | 4.41 | 4.37 | 4.15 | 3.98 | 3.62 | 3.19 | 3.78 | 4.04 | -4.64 |
| **4** | 5.52 | 5.49 | 5.24 | 5.05 | 4.47 | 3.91 | 5.09 | 5.04 | -6.29 |
| **5** | 5.48 | 5.49 | 5.33 | 4.40 | 4.43 | 3.91 | 5.01 | 4.59 | -5.67 |
| **6** | 5.53 | 5.57 | 5.23 | 4.30 | 4.42 | 3.53 | 4.93 | 4.56 | -5.67 |
| **7** | 5.64 | 5.69 | 5.27 | 4.46 | 4.64 | 4.30 | 5.17 | 4.69 | -5.38 |
| **8** | 5.23 | 5.04 | 4.67 | 4.21 | 4.31 | 3.46 | 4.74 | 4.31 | -4.89 |
| **9** | 4.49 | 4.62 | 4.44 | 4.06 | 3.41 | 3.32 | 3.87 | 3.82 | -4.70 |
| **10** | 5.65 | 6.02 | 5.13 | 5.45 | 4.78 | 4.45 | 5.27 | 5.20 | -5.61 |
| **11** | 5.48 | 5.49 | 5.34 | 4.40 | 4.43 | 3.91 | 5.01 | 4.59 | -5.65 |
| **12** | 5.58 | 5.57 | 4.92 | 4.95 | 4.46 | 3.53 | 5.01 | 5.01 | -6.25 |
| **13** | 5.40 | 5.57 | 4.81 | 5.26 | 4.66 | 3.99 | 4.99 | 4.92 | -4.75 |
| **14** | 5.53 | 5.57 | 5.22 | 4.30 | 4.42 | 3.53 | 4.93 | 4.56 | -5.70 |
| **15** | 5.28 | 5.04 | 4.68 | 4.86 | 4.35 | 3.46 | 4.82 | 4.76 | -4.96 |
| **16** | 3.79 | 3.81 | 3.48 | 3.26 | 2.94 | 2.31 | 3.07 | 3.39 | -4.14 |
| **17** | 2.92 | 3.93 | 3.50 | 3.43 | 3.16 | 3.06 | 3.32 | 3.52 | -3.78 |

*Data are estimated solubilities

**Table S2b**. Chromatographic lipophilicty descriptors of benzothiepino[3,2-c]pyridine derivtaves.

| Comp. No. | $R_M^0$_MeOH | *b*_MeOH | *PC1*_MeOH | $C_0$_MeOH | m$R_M$_MeOH | $R_M^0$_Acet | *b*_Acet | *PC1*_Acet | $C_0$_Acet | *m*$R_M$_Acet | $R_M^0$_Diox | *b*_Diox | *PC1*_Diox | $C_0$_Diox | *m*$R_M$_Diox | $R_{M}$_*MLC1* | $R_{M}$_*MLC2* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | 1.25 | -0.01 | -3.65 | 95.06 | 0.07 | 1.16 | -0.02 | -4.96 | 73.22 | -0.07 | 2.94 | -0.04 | -5.00 | 67.77 | -0.31 | 0.37 | 0.12 |
| **2** | 2.90 | -0.03 | -2.79 | 94.64 | 0.14 | 3.55 | -0.04 | -2.08 | 80.22 | 0.12 | 3.39 | -0.05 | -0.98 | 72.79 | -0.10 | 0.39 | 0.17 |
| **3** | 3.33 | -0.03 | 0.33 | 100.60 | 0.35 | 3.18 | -0.04 | 1.02 | 84.99 | 0.28 | 4.28 | -0.06 | 1.59 | 75.69 | 0.04 | 0.44 | 0.23 |
| **4** | 3.75 | -0.04 | 3.19 | 105.31 | 0.54 | 3.94 | -0.05 | 2.71 | 85.93 | 0.39 | 5.19 | -0.07 | 0.30 | 76.43 | 0.10 | 0.53 | 0.30 |
| **5** | 3.49 | -0.03 | 0.76 | 101.07 | 0.38 | 3.61 | -0.04 | 0.78 | 83.85 | 0.27 | 4.89 | -0.06 | 1.71 | 75.63 | 0.04 | 0.57 | 0.34 |
| **6** | 3.79 | -0.04 | 1.45 | 101.51 | 0.43 | 3.68 | -0.04 | 0.23 | 83.10 | 0.25 | 4.95 | -0.07 | 1.17 | 74.51 | -0.03 | 0.57 | 0.34 |
| **7** | 3.68 | -0.04 | -0.13 | 98.75 | 0.33 | 4.09 | -0.05 | 1.12 | 83.68 | 0.30 | 4.74 | -0.06 | 0.86 | 75.35 | 0.02 | 0.57 | 0.37 |
| **8** | 2.65 | -0.03 | -1.72 | 97.71 | 0.21 | 2.69 | -0.03 | -1.67 | 81.33 | 0.13 | 4.34 | -0.06 | -1.10 | 72.43 | -0.15 | 0.46 | 0.24 |
| **9** | 3.10 | -0.03 | -0.28 | 99.94 | 0.31 | 3.25 | -0.04 | 0.37 | 83.72 | 0.24 | 4.05 | -0.05 | -0.07 | 73.96 | -0.06 | 0.54 | 0.32 |
| **10** | 4.02 | -0.04 | 1.76 | 101.45 | 0.45 | 4.09 | -0.05 | 2.32 | 84.99 | 0.36 | 4.47 | -0.06 | 1.04 | 75.70 | 0.04 | 0.62 | 0.37 |
| **11** | 3.74 | -0.04 | 1.82 | 102.46 | 0.45 | 3.78 | -0.04 | 2.22 | 85.33 | 0.35 | 4.50 | -0.06 | -1.88 | 75.22 | 0.01 | 0.53 | 0.30 |
| **12** | 3.85 | -0.04 | 3.90 | 106.40 | 0.59 | 3.84 | -0.05 | 1.76 | 84.67 | 0.32 | 5.16 | -0.07 | 1.31 | 74.95 | 0.00 | 0.53 | 0.30 |
| **13** | 3.72 | -0.04 | -1.18 | 96.71 | 0.26 | 4.66 | -0.06 | 0.72 | 82.68 | 0.29 | 5.49 | -0.07 | -0.77 | 73.52 | -0.11 | 0.54 | 0.32 |
| **14** | 4.01 | -0.04 | 2.24 | 102.41 | 0.49 | 4.07 | -0.05 | 1.29 | 83.73 | 0.30 | 4.61 | -0.06 | -0.29 | 75.21 | 0.01 | 0.52 | 0.30 |
| **15** | 3.23 | -0.03 | -1.52 | 96.90 | 0.23 | 4.33 | -0.05 | -0.66 | 81.27 | 0.20 | 5.11 | -0.07 | -2.16 | 73.87 | -0.08 | 0.49 | 0.32 |
| **16** | 2.57 | -0.03 | -1.50 | 98.56 | 0.22 | 2.94 | -0.04 | -3.17 | 78.68 | 0.04 | 3.36 | -0.05 | 2.63 | 72.08 | -0.14 | 0.37 | 0.19 |
| **17** | 2.58 | -0.03 | -2.68 | 95.36 | 0.15 | 2.92 | -0.04 | -2.02 | 80.43 | 0.11 | 3.54 | -0.05 | 1.65 | 73.93 | -0.05 | 0.35 | 0.17 |

**Table S3.** SRD scores for standardized (Std), range scaled (Rng) and Rank (Rnk) lipophilicity data.

| Std | | Rng | | Rnk | |
|---|---|---|---|---|---|
| **Variable** | **SRD** | **Variable** | **SRD** | **Variable** | **SRD** |
| XlogP2 | 13.89 | XlogP2 | 13.89 | milogP | 13.89 |
| *PC1*_Acet | 13.89 | *PC1*_Acet | 13.89 | XlogP2 | 13.89 |
| milogP | 15.28 | milogP | 15.28 | AlogP | 15.97 |
| $mR_M$_Acet | 15.28 | $mR_M$_Acet | 15.28 | XlogP3 | 16.67 |
| AlogP | 15.97 | AlogP | 15.97 | *PC1*_Acetone | 16.67 |
| XlogP3 | 19.44 | XlogP3 | 19.44 | KOWWIN | 18.06 |
| $R_M^0$_MeOH | 19.44 | $R_M^0$_MeOH | 19.44 | $mR_M$_Acetone | 18.06 |
| mlogP | 20.14 | mlogP | 20.14 | $R_M^0$_MeOH | 19.44 |
| KOWWIN | 20.83 | KOWWIN | 20.83 | mlogP | 20.14 |
| AClogP | 20.83 | AClogP | 20.83 | AClogP | 20.83 |
| AlogpS | 20.83 | AlogpS | 20.83 | AlogpS | 22.22 |
| AlogPs | 23.61 | AlogPs | 23.61 | $mR_M$_MeOH | 22.22 |
| *b*_MeOH | 23.61 | *b*_MeOH | 23.61 | *b*_MeOH | 23.61 |
| $mR_M$_MeOH | 23.61 | $mR_M$_MeOH | 23.61 | *PC1*_MeOH | 23.61 |
| $C_0$_Acet | 23.61 | $C_0$_Acet | 23.61 | AlogPs | 25.00 |
| $C_0$_Diox | 23.61 | $C_0$_Diox | 23.61 | $C_0$_Acet | 26.39 |
| *PC1*_MeOH | 25.00 | *PC1*_MeOH | 25.00 | $C_0$_Diox | 26.39 |
| $mR_M$_Diox | 25.00 | $mR_M$_Diox | 25.00 | $mR_M$_Diox | 26.39 |
| $R_M^0$_Diox | 26.39 | $R_M^0$_Diox | 26.39 | $R_M^0$_Diox | 27.78 |
| $C_0$_MeOH | 31.94 | $C_0$_MeOH | 31.94 | $C_0$_MeOH | 30.56 |
| $R_M^0$_Acet | 31.94 | $R_M^0$_Acet | 31.94 | $R_M^0$_Acet | 31.94 |
| *b*_Diox | 33.33 | b_Diox | 33.33 | *b*_Diox | 31.94 |
| $R_M$_MELC1 | 33.33 | $R_M$_MELC1 | 33.33 | $R_M$_MELC1 | 31.94 |
| *b*_Acet | 34.72 | *b*_Acet | 34.72 | $R_M$_MELC2 | 34.03 |
| $R_M$_MELC2 | 36.11 | $R_M$_MELC2 | 36.11 | *b*_Acet | 34.72 |
| *PC1*_Diox | 59.72 | *PC1*_Diox | 59.72 | *PC1*_Diox | 59.72 |

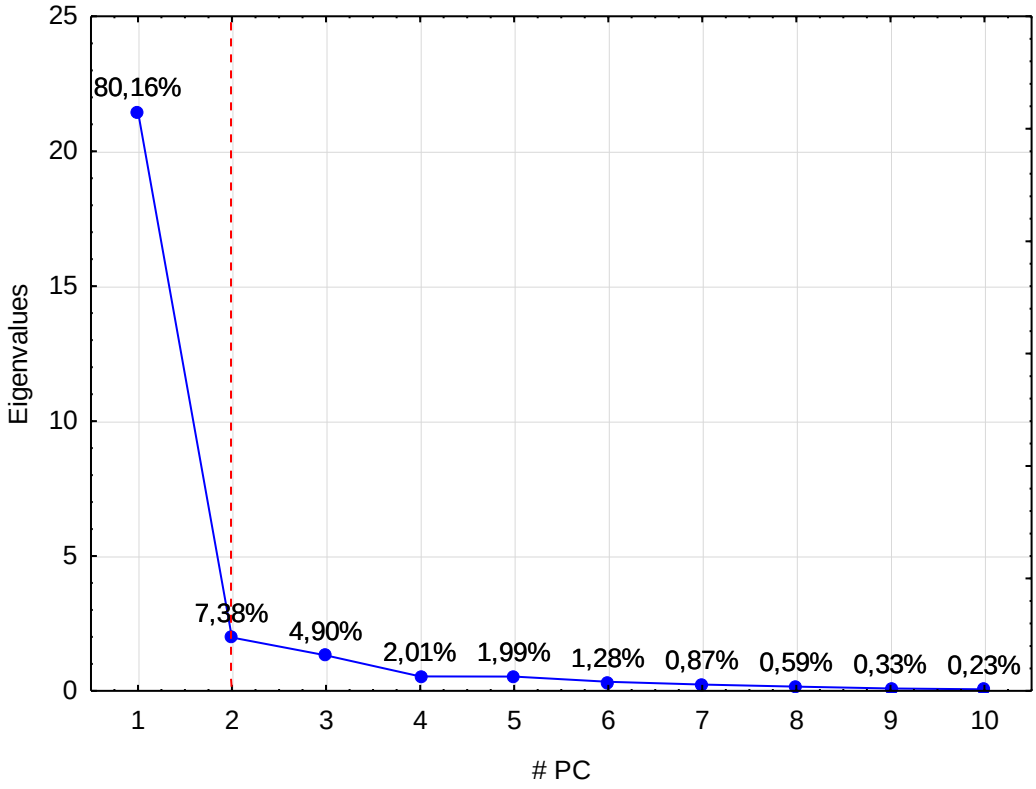


**Figure S1** Eigenvalues scree plot showing distribution of data variability by principal components. Following the "broken stick" rule the first two principal components can be selected to efficiently describe retention data structure.

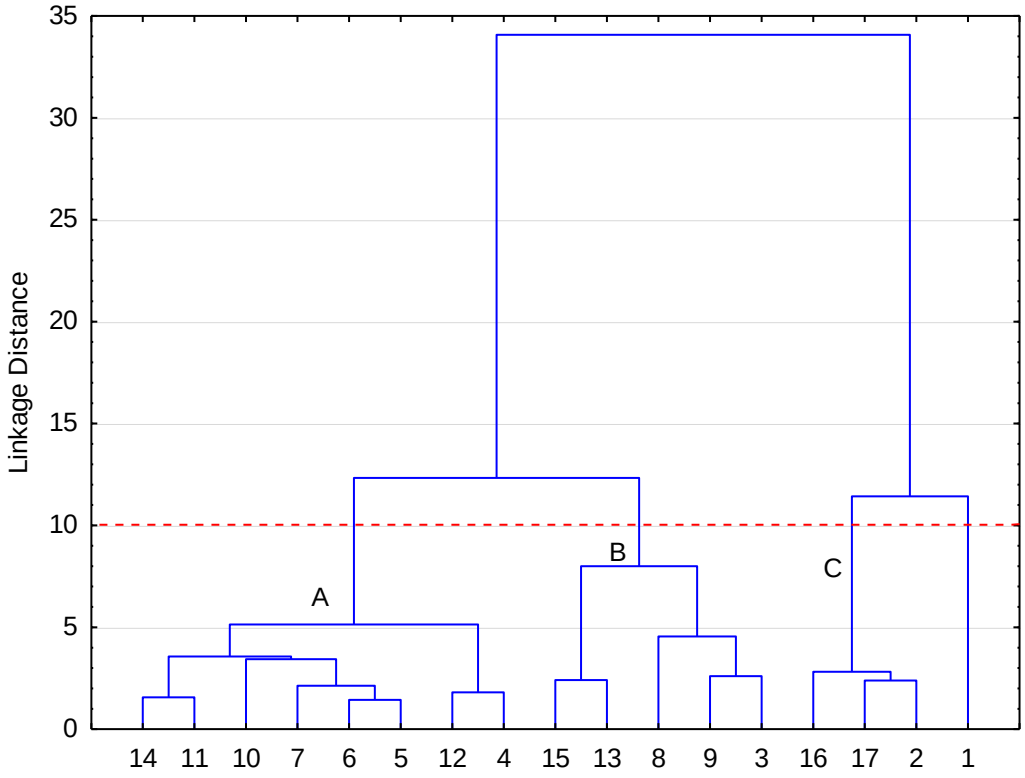


**Figure S2** HCA of retention data of compounds. Three clusters (A, B and C) can be observed at linkage distance of 10 units and one outlier (compound no. 1). For numeration and chemical structures of compounds see Table 1 in the manuscript