Supplementary Information

Synthesis, Characterization and Preliminary Study on Acetylpyrazine N(4)Butylthiosemicarbazone as a Potential CDK2 Inhibitor Combined with DFT Calculations

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Figure S1. Numbering used for assignment of 1H and 13C NMR chemical shift signals for APBT.

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**Figure S2.** Bond length correlation coefficient of APBT.

**Figure S3.** Optimized geometries of the reactants and product involved in the chemical reaction calculated at the B3LYP/6-311++G(d,p).
Table S1. The experimental and calculated geometric parameters of APBT

| Geometric parameter | Experimental$^1$ | Calculated B3LYP/6-311++G(d,p) |
|---------------------|-----------------|-------------------------------|
| Bond length / Å     |                 |                               |
| S19–C18             | 1.680           | 1.681                         |
| N6–C5               | 1.329           | 1.331                         |
| N1–C6               | 1.347           | 1.342                         |
| N3–C2               | 1.342           | 1.336                         |
| N3–C4               | 1.337           | 1.344                         |
| N15–N16             | 1.366           | 1.349                         |
| N15–C10             | 1.284           | 1.296                         |
| N16–C18             | 1.373           | 1.386                         |
| N20–C18             | 1.337           | 1.343                         |
| N20–C22             | 1.409           | 1.458                         |
| C4–C5               | 1.406           | 1.411                         |
| C1–C2               | 1.383           | 1.393                         |
| C4–C10              | 1.485           | 1.481                         |
| C10–C11             | 1.500           | 1.506                         |
| Bond angle / degree |                 |                               |
| C5–N6–C1            | 116.5           | 116.5                         |
| C2–N3–C4            | 116.5           | 117.1                         |
| N16–N15–C10         | 120.4           | 118.6                         |
| N15–N16–C18         | 117.9           | 121.9                         |
| C18–N20–C22         | 133.3           | 125.1                         |
| N15–C10–C4          | 122.1           | 122.6                         |
| N6–C1–C2            | 121.4           | 121.6                         |
| N3–C2–C1            | 122.4           | 122.0                         |
| N3–C4–C10           | 121.1           | 120.2                         |
| C10–C4–C5           | 121.8           | 122.4                         |
| N15–C10–C4          | 114.0           | 116.5                         |
| N15–C10–C11         | 126.6           | 123.9                         |
| C4–C10–C11          | 119.4           | 119.6                         |
| S19–C18–N16         | 119.1           | 118.3                         |
| S19–C18–N20         | 127.4           | 127.0                         |
| N16–C18–N20         | 113.4           | 114.7                         |
| Mode No. | Experimental frequency / cm\(^{-1}\) | Calculated frequency / cm\(^{-1}\) | Intensity | Vibrational assignment (PED ≥ 10 / %) |
|----------|-------------------------------------|-----------------------------------|-----------|--------------------------------------|
|          |                                    | Unscaled                          | Scaled    |                                      |
| 1        | 3363                                | 3587                              | 3453      | 53.59 v\((N20H21)\) (99)            |
| 2        | 3219                                | 3571                              | 3438      | 35.78 v\((N16H17)\) (99)            |
| 3        | 3096                                | 3210                              | 3090      | 4.30 v\((C5H9)\) (96)               |
| 4        | 3080                                | 3192                              | 3073      | 48.20 v\((C1H7)\) (93)              |
| 5        | –                                   | 3182                              | 3063      | 1.94 v\((C11H13)\) (93)            |
| 6        | –                                   | 3172                              | 3054      | 10.96 v\((C1H7)\) (95)              |
| 7        | 3004                                | 3139                              | 3022      | 4.76 v\((C22H24)\) (86)            |
| 8        | 2995                                | 3117                              | 3001      | 45.24 v\((C31H33)\) (84)           |
| 9        | –                                   | 3115                              | 2999      | 45.35 v\((C31H32)\) (93)           |
| 10       | –                                   | 3084                              | 2969      | 25.46 v\((C25H26)\) (80)           |
| 11       | –                                   | 3083                              | 2968      | 11.05 v\((C11H12)\) (97)           |
| 12       | –                                   | 3064                              | 2950      | 25.24 v\((C28H29)\) (78)           |
| 13       | 2929                                | 3049                              | 2935      | 40.63 v\((C22H23)\) (85)           |
| 14       | –                                   | 3046                              | 2932      | 15.59 v\((C31H32)\) (94)           |
| 15       | –                                   | 3033                              | 2920      | 24.87 v\((C25H27)\) (85)           |
| 16       | –                                   | 3031                              | 2918      | 6.97 v\((C11H12)\) (93)            |
| 17       | 2867                                | 3024                              | 2911      | 25.51 v\((C28H29)\) (13)           |
| 18       | 1630                                | 1660                              | 1598      | 63.95 v\((N15C11)\) (63)           |
| 19       | 1599                                | 1612                              | 1552      | 29.64 v\((N15C10)\) (52) + δ\((H8C2N3)\) (21) |
| 20       | –                                   | 1588                              | 1529      | 278.74 v\((N20C18)\) (53) + δ\((H21N20C22)\) (30) |
| 21       | 1504                                | 1582                              | 1523      | 139.60 v\((N6C5)\) (69)            |
| 22       | 1470                                | 1541                              | 1484      | 264.09 δ\((H17N16N15)\) (53)       |
| 23       | 1464                                | 1522                              | 1465      | 3.67 δ\((H32C31H33)\) (68) + τ\((H29C28C31H33)\) (10) |
| 24       | –                                   | 1518                              | 1461      | 6.14 δ\((H26C25H27)\) (70) + τ\((H29C28N25C22)\) (12) |
| 25       | –                                   | 1514                              | 1458      | 8.68 δ\((H13C11H14)\) (81) + τ\((C11H12C10H13)\) (13) |
| 26       | –                                   | 1508                              | 1452      | 60.63 δ\((H26C25H27)\) (57)        |
|   |   |   |   |   |
|---|---|---|---|---|
| 27 | – | 1506 | 1450 | 55.80 \(\delta([H26C25H27])\) \((56)\) |
| 28 | – | 1503 | 1447 | 0.97 \(\gamma([H26C25H28])\) \((65)\) |
| 29 | – | 1495 | 1439 | 48.60 \(\delta([H23C22H24]) + \tau([C11H12C10H14])\) \((14)\) |
| 30 | 1421 | 1482 | 1427 | 104.67 \(\delta([H13C11C10]) + \tau([C11H12C10H14])\) \((23)\) |
| 31 | 1403 | 1446 | 1392 | 52.93 \(\delta([H7C1N6])\) \((38)\) |
| 32 | – | 1436 | 1382 | 3.78 \(\gamma([H23C22H24])\) \((65)\) |
| 33 | – | 1428 | 1375 | 24.58 \(\tau([H24C22C21C18])\) \((53)\) |
| 34 | – | 1409 | 1356 | 7.95 \(\gamma([H12C11H14])\) \((78)\) |
| 35 | – | 1393 | 1341 | 43.04 \(\delta([H21N20C21])\) \((41)\) |
| 36 | 1318 | 1387 | 1335 | 36.12 \(\tau([H29C28C31H33])\) \((46)\) |
| 37 | 1297 | 1355 | 1304 | 2.83 \(\delta([H26C25C28])\) \((42) + \tau([H34C31C28C25])\) \((10)\) |
| 38 | 1255 | 1349 | 1299 | 25.77 \(\gamma([H23C22N20])\) \((53) + \delta([H23C22N20])\) \((12)\) |
| 39 | – | 1329 | 1279 | 94.59 \(\nu([C4C5])\) \((17) + \delta([H12N20N22])\) \((12)\) |
| 40 | – | 1323 | 1274 | 11.05 \(\nu([C4C5])\) \((28) + \delta([H8C2N3])\) \((51)\) |
| 41 | – | 1300 | 1252 | 17.36 \(\gamma([H26C25C28])\) \((24) + \tau([H23C22N20C18])\) \((43)\) |
| 42 | 1224 | 1276 | 1228 | 113.42 \(\delta([H23C22C20])\) \((39)\) |
| 43 | – | 1263 | 1216 | 72.73 \(\nu([N3C2])\) \((70)\) |
| 44 | 1176 | 1217 | 1172 | 359.38 \(\nu([N16C18])\) \((41) + \tau([H29C28C25C22])\) \((10)\) |
| 45 | – | 1207 | 1162 | 13.16 \(\nu([C1C6])\) \((18) + \delta([H9C5N6])\) \((13)\) |
| 46 | 1113 | 1180 | 1136 | 33.01 \(\nu([N15N160])\) \((17) + \tau([H29C28C25C22])\) \((26)\) |
| 47 | 1104 | 1171 | 1127 | 60.45 \(\nu([N15N16])\) \((38)\) |
| 48 | – | 1137 | 1095 | 16.91 \([\nu([C2C2C25])\) \((30) + \delta([C25C22N20])\) \((12) + \tau([H34C31C28C25])\) \((31)\) |
| 49 | – | 1124 | 1082 | 14.80 \(\delta([H13N11N10])\) \((10) + \delta([C2C1N6])\) \((14) + \tau([C11H12C10H14])\) \((11)\) |
| 50 | 1064 | 1096 | 1055 | 55.20 \(\nu([C2C2C25]) + \nu([S19C18])\) \((30) + \tau([H33C31C28C25])\) \((10)\) |
| 51 | – | 1076 | 1036 | 10.99 \(\nu([C1C2])\) \((62)\) |
| 52 | – | 1073 | 1033 | 16.58 \(\nu([C28C31])\) \((73)\) |
| 53 | 1008 | 1055 | 1016 | 0.26 \(\gamma([H13C11C14])\) \((14) + \tau([C11H12C10H13])\) \((72)\) |
| 54 | – | 1030 | 992 | 33.21 \(\delta([C10N15N16])\) \((21) + \delta([C2N3C4])\) \((19) + \delta([C1C2N3])\) \((41)\) |
| 55 | 960 | 992 | 955 | 3.40 \(\nu([C10C11])\) \((38) + \nu([H23C22H24])\) \((10)\) |
| 56  | –   | 984  | 947  | 0.09  | v[(C22C25)] (30) + τ[(H7C12H8)] (86) |
| 57  | –   | 983  | 946  | 3.21  | τ[(H34C31C28C25)] (15) |
| 58  | 928 | 963  | 927  | 0.33  | τ[(H8C2C1N6)] (66) |
| 59  | –   | 956  | 920  | 5.13  | τ[(H33C31C28C25)] (48) |
| 60  | 848 | 888  | 855  | 2.81  | v[(C28C25)] (61) + τ[(H22C25C20C23)] (10) |
| 61  | –   | 868  | 836  | 13.51 | τ[(H7C1N6C5)] (91) |
| 62  | 800 | 856  | 824  | 29.52 | v[(S19C18)] (25) + δ[(C1C2N3)] (14) |
| 63  | 761 | 798  | 768  | 7.33  | τ[(H29C28C31H33)] (37) |
| 64  | –   | 788  | 759  | 1.30  | τ[(H32C31C28C25)] (20) |
| 65  | –   | 777  | 748  | 1.43  | τ[(C2N3C4C5)] (77) |
| 66  | 704 | 756  | 728  | 8.20  | τ[(C22C25N20H23)] (58) |
| 67  | 641 | 672  | 647  | 7.31  | v[(S19C18)] (11) + δ[(C1C10N15)] (46) |
| 68  | –   | 644  | 620  | 8.39  | τ[(C18N16N20S19)] (80) |
| 69  | –   | 626  | 603  | 0.52  | δ[(C1N6C5)] (80) |
| 70  | 585 | 599  | 577  | 12.59 | δ[(C18N20C22)] (23) + τ[(C2C1N6C5)] (25) |
| 71  | –   | 596  | 574  | 27.96 | γ[(N20C18S19)] (12) + τ[(C11C4N15C10)] (41) |
| 72  | 537 | 565  | 544  | 41.93 | τ[(H21N20C18S19)] (80) |
| 73  | 529 | 542  | 522  | 2.57  | δ[(C18N16N15)] (45) |
| 74  | 497 | 521  | 502  | 47.10 | τ[(H17N16C18S19)] (76) |
| 75  | 481 | 480  | 462  | 36.55 | τ[(N3C2C1N6)] (83) |
| 76  | –   | 468  | 451  | 9.68  | γ[(C22C25C28)] (45) |
| 77  | 417 | 423  | 407  | 12.83 | τ[(C21N6C5)] (84) |
| 78  | –   | 418  | 402  | 10.69 | δ[(C5C4C10)] (56) |
| 79  | –   | 361  | 348  | 1.38  | δ[(C25C28C31)] (57) |
| 80  | –   | 313  | 301  | 0.80  | δ[(C11C10N15)] (62) |
| 81  | –   | 310  | 298  | 4.31  | γ[(C22C25C28)] (41) + τ[(H33C31C28C25)] (12) |
| 82  | –   | 292  | 281  | 0.10  | τ[(C410N15N16)] (53) |
| 83  | –   | 279  | 269  | 2.87  | δ[(N20C18S19)] (28) + τ[(H33C31C28C25)] (31) |
| 84  | –   | 232  | 223  | 0.50  | γ[(C18N20C22)] (45) + τ[(H29C28C25C22)] (14) |
| PED     | ν: stretching; δ: in-plane bending; γ: out-of-plane bending; τ: torsion. | Scaling factor = 0.9627. |
|---------|-----------------------------------------------------------------------|--------------------------|
| 85      | 211 203 4.09 δ[(C2C1N6)] (10) + γ[(C18C20C22)] (18) + τ[(H29C28C25C22)] (24) |                         |
| 86      | 177 170 9.55 δ[(C5C4C10)] (64)                                        |                         |
| 87      | 169 163 1.12 τ[(H12C11C10C4)] (79)                                    |                         |
| 88      | 139 134 1.78 τ[(H12C11C10C4)] (13) + τ[(C10C4C5N6)] (67)               |                         |
| 89      | 116 112 0.30 τ[(C28C25C22N20)] (57)                                   |                         |
| 90      | 108 104 0.45 τ[(C10N15N16C18)] (56) + τ[(N4N10C15N16)] (10)            |                         |
| 91      | 72   69  1.33 γ[(C10N15N16)] (59)                                     |                         |
| 92      | 59   57  0.45 τ[(C18N20C22C25)] (63)                                   |                         |
| 93      | 48   46  1.89 τ[(N3C4C10N15)] (16) + τ[(C4C10N15N16)] (66)             |                         |
| 94      | 42   40  0.26 τ[(C31C28C25C22)] (10) + τ[(C28C25C22N20)] (57)          |                         |
| 95      | 27   26  0.12 τ[(C22N20C18N16)] (65)                                   |                         |
| 96      | 18   17  0.65 τ[(N3C4C10N15)] (84)                                    |                         |
Figure S4. $^1$H NMR (400 MHz, DMSO-$d_6$) spectrum of APBT.
Figure S5. $^{13}$C NMR (400 MHz, DMSO-$d_6$) spectrum of APBT.

References

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