

Supporting Information

Structural Insights of Three 2,4-Disubstituted Dihydropyrimidine-5-carbonitriles as Potential Dihydrofolate Reductase Inhibitors

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Checkcif report for compound 1

Datablock

| | | |
|--|---|--------------------|
| Bond precision: | C-C = 0.0052 Å | Wavelength=1.54184 |
| Cell: | a=12.5792(7) b=9.5493(5) c=13.3158(8) | |
| | alpha=90 beta=106.432(7) gamma=90 | |
| Temperature: 293 K | | |
| | Calculated | Reported |
| Volume | 1534.20(16) | 1534.20(16) |
| Space group | P 21/n | P 21/n |
| Hall group | -P 2yn | -P 2yn |
| Moiety formula | C15 H14 N4 O3 S | C15 H14 N4 O3 S1 |
| Sum formula | C15 H14 N4 O3 S | C15 H14 N4 O3 S |
| Mr | 330.36 | 330.36 |
| Dx,g cm-3 | 1.430 | 1.430 |
| Z | 4 | 4 |
| Mu (mm-1) | 2.068 | 2.068 |
| F000 | 688.0 | 688.0 |
| F000' | 691.37 | |
| h,k,lmax | 15,12,16 | 15,11,16 |
| Nref | 3194 | 3194 |
| Tmin,Tmax | 0.742,0.848 | 0.900,1.000 |
| Tmin' | 0.718 | |
| Correction method= # Reported T Limits: Tmin=0.900 Tmax=1.000 AbsCorr = MULTI-SCAN | | |
| Data completeness= 1.000 | Theta(max)= 75.706 | |
| R(reflections)= 0.0569(1849) | wR2(reflections)= 0.1479(3163) | |
| S = 1.030 | Npar= 213 | |

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

Alert level C

[PLAT242_ALERT_2_C](#) Low 'MainMol' Ueq as Compared to Neighbors of N4 Check
[PLAT340_ALERT_3_C](#) Low Bond Precision on C-C Bonds 0.00515 Å.

[PLAT906_ALERT_3_C](#) Large K Value in the Analysis of Variance 7.900 Check

Alert level G

[PLAT199_ALERT_1_G](#) Reported _cell_measurement_temperature (K) 293 Check
[PLAT200_ALERT_1_G](#) Reported _diffn_ambient_temperature (K) 293 Check
[PLAT883_ALERT_1_G](#) No Info/Value for _atom_sites_solution_primary . Please Do !
[PLAT912_ALERT_4_G](#) Missing # of FCF Reflections Above STh/L= 0.600 30 Note
[PLAT941_ALERT_3_G](#) Average HKL Measurement Multiplicity 4.9 Low
[PLAT978_ALERT_2_G](#) Number C-C Bonds with Positive Residual Density. 0 Info

0 **ALERT level A** = Most likely a serious problem - resolve or explain

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3 ALERT type 1 CIF construction/syntax error, inconsistent or missing data

2 ALERT type 2 Indicator that the structure model may be wrong or deficient

3 ALERT type 3 Indicator that the structure quality may be low

1 ALERT type 4 Improvement, methodology, query or suggestion

0 ALERT type 5 Informative message, check

Checkcif report for compound 2

Datablock

Bond precision: C-C = 0.0080 A Wavelength=1.54184

Cell: a=18.3676(7) b=5.7996(2) c=31.8592(12)

alpha=90 beta=95.343(4) gamma=90

Temperature: 293 K

| | Calculated | Reported |
|----------------|-----------------|------------------|
| Volume | 3379.1(2) | 3379.0(2) |
| Space group | C 2/c | C 2/c |
| Hall group | -C 2yc | -C 2yc |
| Moiety formula | C16 H16 N4 O3 S | C16 H16 N4 O3 S1 |
| Sum formula | C16 H16 N4 O3 S | C16 H16 N4 O3 S |
| Mr | 344.39 | 344.39 |
| Dx,g cm-3 | 1.354 | 1.354 |
| Z | 8 | 8 |
| Mu (mm-1) | 1.899 | 1.899 |
| F000 | 1440.0 | 1440.0 |
| F000' | 1446.88 | |
| h,k,lmax | 22,7,40 | 22,7,40 |
| Nref | 3516 | 3516 |
| Tmin,Tmax | 0.898,0.916 | 0.871,1.000 |
| Tmin' | 0.732 | |

Correction method= # Reported T Limits: Tmin=0.871 Tmax=1.000 AbsCorr =
MULTI-SCAN

Data completeness= 1.000 Theta(max)= 75.711

R(reflections)= 0.0766(1660) wR2(reflections)= 0.2358(3418)

S = 0.998 Npar= 211

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

● Alert level C

[PLAT026_ALERT_3_C](#) Ratio Observed / Unique Reflections (too) Low .. 47% Check
[PLAT220_ALERT_2_C](#) NonSolvent Resd 1 C Ueq(max)/Ueq(min) Range 3.9 Ratio
[PLAT234_ALERT_4_C](#) Large Hirshfeld Difference C6 --C7 . 0.16 Ang.
[PLAT242_ALERT_2_C](#) Low 'MainMol' Ueq as Compared to Neighbors of N4 Check
[PLAT242_ALERT_2_C](#) Low 'MainMol' Ueq as Compared to Neighbors of C6 Check
[PLAT340_ALERT_3_C](#) Low Bond Precision on C-C Bonds 0.008 Ang.
[PLAT906_ALERT_3_C](#) Large K Value in the Analysis of Variance 8.039 Check
[PLAT906_ALERT_3_C](#) Large K Value in the Analysis of Variance 2.153 Check
[PLAT911_ALERT_3_C](#) Missing FCF Refl Between Thmin & STh/L= 0.600 7 Report

● Alert level G

[PLAT002_ALERT_2_G](#) Number of Distance or Angle Restraints on AtSite 3 Note
[PLAT171_ALERT_4_G](#) The CIF-Embedded .res File Contains EADP Records 2 Report
[PLAT172_ALERT_4_G](#) The CIF-Embedded .res File Contains DFIX Records 2 Report
[PLAT176_ALERT_4_G](#) The CIF-Embedded .res File Contains SADI Records 2 Report
[PLAT199_ALERT_1_G](#) Reported _cell_measurement_temperature (K) 293 Check
[PLAT200_ALERT_1_G](#) Reported _diffrn_ambient_temperature (K) 293 Check
[PLAT860_ALERT_3_G](#) Number of Least-Squares Restraints 2 Note
[PLAT883_ALERT_1_G](#) No Info/Value for _atom_sites_solution_primary . Please Do !
[PLAT912_ALERT_4_G](#) Missing # of FCF Reflections Above STh/L= 0.600 91 Note
[PLAT933_ALERT_2_G](#) Number of OMIT Records in Embedded .res File ... 8 Note
[PLAT941_ALERT_3_G](#) Average HKL Measurement Multiplicity 4.9 Low
[PLAT978_ALERT_2_G](#) Number C-C Bonds with Positive Residual Density. 1 Info

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Checkcif report for compound 3

Datablock

| | | |
|--------------------|------------------|--------------------|
| Bond precision: | C-C = 0.0036 A | Wavelength=1.54184 |
| Cell: | a=7.1456(4) | b=10.8642(6) |
| | alpha=104.672(5) | beta=108.159(5) |
| | | gamma=95.421(5) |
| Temperature: 293 K | | |
| | Calculated | Reported |
| Volume | 788.84(9) | 788.84(8) |
| Space group | P -1 | P -1 |

| | | |
|----------------|-----------------------|-----------------------|
| Hall group | -P 1 | -P 1 |
| Moiety formula | C15 H15 N3 O2 S, H2 O | C15 H15 N3 O2 S, H2 O |
| Sum formula | C15 H17 N3 O3 S | C15 H17 N3 O3 S |
| Mr | 319.38 | 319.38 |
| Dx,g cm-3 | 1.345 | 1.345 |
| Z | 2 | 2 |
| Mu (mm-1) | 1.968 | 1.968 |
| F000 | 336.0 | 336.0 |
| F000' | 337.63 | |
| h,k,lmax | 8,13,14 | 8,13,13 |
| Nref | 3264 | 3265 |
| Tmin,Tmax | 0.754,0.821 | 0.966,1.000 |
| Tmin' | 0.571 | |

Correction method= # Reported T Limits: Tmin=0.966 Tmax=1.000 AbsCorr =
MULTI-SCAN

Data completeness= 1.000 Theta(max)= 75.547
R(reflections)= 0.0432(2299) wR2(reflections)= 0.1210(3220)
S = 1.035 Npar= 212

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Click on the hyperlinks for more details of the test.

Alert level C

[PLAT241_ALERT_2_C](#) High 'MainMol' Ueq as Compared to Neighbors of C8 Check
[PLAT906_ALERT_3_C](#) Large K Value in the Analysis of Variance 2.891 Check

Alert level G

[PLAT002_ALERT_2_G](#) Number of Distance or Angle Restraints on AtSite 3 Note
[PLAT154_ALERT_1_G](#) The s.u.'s on the Cell Angles are Equal ..(Note) 0.005 Degree
[PLAT172_ALERT_4_G](#) The CIF-Embedded .res File Contains DFIX Records 2 Report
[PLAT199_ALERT_1_G](#) Reported _cell_measurement_temperature (K) 293 Check
[PLAT200_ALERT_1_G](#) Reported _diffn_ambient_temperature (K) 293 Check
[PLAT860_ALERT_3_G](#) Number of Least-Squares Restraints 2 Note
[PLAT883_ALERT_1_G](#) No Info/Value for _atom_sites_solution_primary . Please Do !
[PLAT912_ALERT_4_G](#) Missing # of FCF Reflections Above STh/L= 0.600 37 Note
[PLAT933_ALERT_2_G](#) Number of OMIT Records in Embedded .res File ... 1 Note
[PLAT941_ALERT_3_G](#) Average HKL Measurement Multiplicity 3.8 Low
[PLAT978_ALERT_2_G](#) Number C-C Bonds with Positive Residual Density. 2 Info

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