

Catalyst-free synthesis of benzofuran-fused pyrido[4,3-*d*]pyrimidines from 2-(2-hydroxyaryl)acetonitrile and 4,6-dichloropyrimidine-5-carbaldehyde through domino condensation reactions

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Supporting Information

List of contents

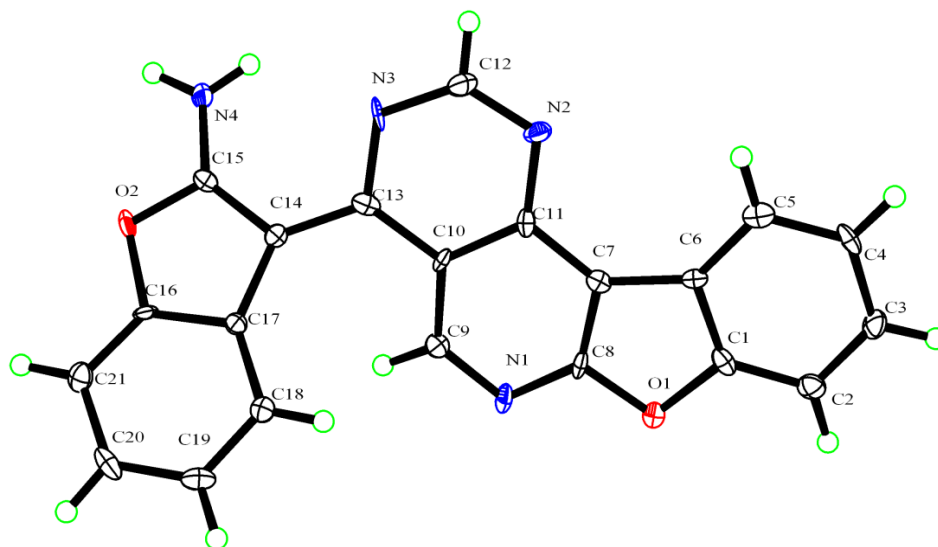
Experimental Section.....	2
X-ray crystallography of compound 3a and 3b	3-4
¹ H NMR and ¹³ C NMR spectra of 3a-3p	5-20

Experimental Section

General experimental: Analytical thin layer chromatography (TLC) was HSGF254 (0.15-0.2mm thickness, Yantai Huiyou Company, China). Column chromatography was carried out on silica gel (200-300 mesh). Proton and carbon magnetic resonance spectra (^1H NMR and ^{13}C NMR) were recorded on Varian Mercury-300/400 and Varian Mercury-400/500 spectrometers. Tetramethylsilane (TMS) was used as internal standard. Chemical shifts (δ) are reported in parts per million (ppm). Data are reported as follows: chemical shift, multiplicity (brs = broad singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, td = triplet of doublet, m = multiple, s = singlet and t = triplet), coupling constants (Hz). HRMS spectra were recorded on a Finnigan/MAT-95 spectrometer. Melting points were measured by Büchi 510 melting point apparatus and were uncorrected.

General procedure for the synthesis of compounds 3a-3p: 2-(2-hydroxyphenyl)acetonitrile **1a** (53 mg, 0.4 mmol), 4,6-dichloropyrimidine-5-carbaldehyde **2** (35 mg, 0.2mmol), Cs_2CO_3 (195 mg, 0.6 mmol) and anhydrous DMF (3 mL) were added to an oven-dried 25 mL two-necked reaction flask. Then the system was degassed and filled with nitrogen. The reaction mixture was stirred and heated at 100°C for 1h. After completion of the reaction, the resulting solution was cooled to room temperature, the mixture was filtrated and the solvent was removed afterwards under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (5:1) as the eluent to provide the desired products **3a**.

X-ray crystallography of compound 3a and 3b



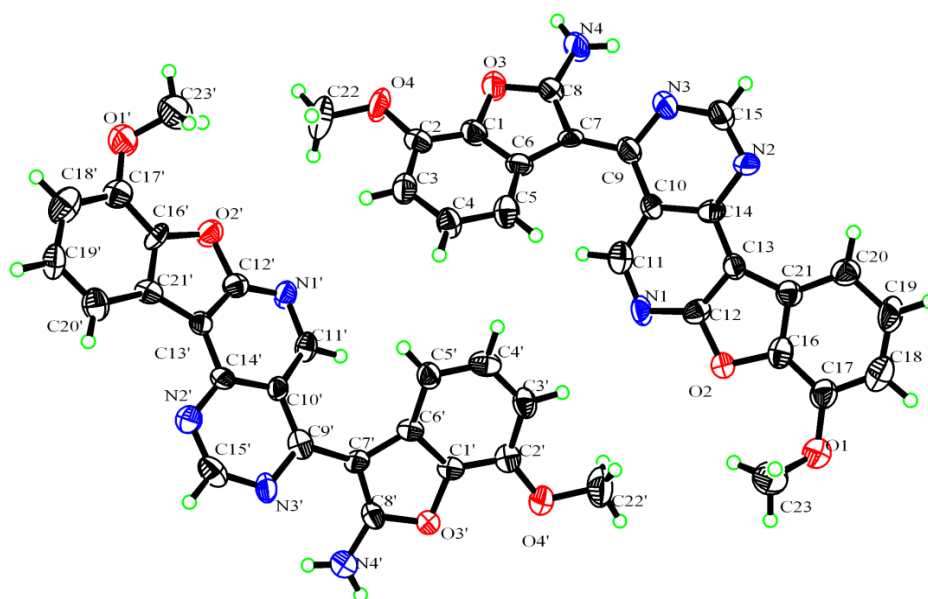
3a

A specimen of $C_{21}HN_4O_2$, approximate dimensions 0.050 mm x 0.050 mm x 0.500 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 2.71 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using an orthorhombic unit cell yielded a total of 6487 reflections to a maximum θ angle of 24.99° (0.84 Å resolution), of which 2210 were independent (average redundancy 2.935, completeness = 96.4%, $R_{int} = 5.83\%$, $R_{sig} = 9.53\%$) and 1652 (74.75%) were greater than $2\sigma(F^2)$. The final cell constants of $a = 3.7225(6)$ Å, $b = 14.857(3)$ Å, $c = 27.524(4)$ Å, volume = 1522.2(4) Å³, are based upon the refinement of the XYZ-centroids of 1846 reflections above $20\sigma(I)$ with $5.218^\circ < 2\theta < 55.03^\circ$. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.689. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9511 and 0.9950.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 21 21 21, with $Z = 4$ for the formula unit, $C_{21}HN_4O_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 244 variables converged at $R1 = 9.33\%$, for the observed data and $wR2 = 24.01\%$ for all data. The goodness-of-fit was 1.291. The largest peak in the final difference electron density synthesis was 0.528 e/Å³ and the largest hole was -0.509 e/Å³ with an RMS deviation of 0.108 e/Å³. On the basis of the final model, the calculated density was 1.489 g/cm³ and $F(000)$, 684 e⁻.

CCDC- 945367 (3a) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



3b

A specimen of $C_{46}H_{34}N_8O_8$, approximate dimensions 0.020 mm x 0.020 mm x 0.250 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 7.18 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 14771 reflections to a maximum θ angle of 25.00° (0.84 Å resolution), of which 6239 were independent (average redundancy 2.368, completeness = 97.3%, $R_{int} = 31.43\%$, $R_{sig} = 57.48\%$) and 1246 (19.97%) were greater than $2\sigma(F^2)$. The final cell constants of $a = 3.8285(15)$ Å, $b = 21.348(8)$ Å, $c = 22.566(10)$ Å, $\alpha = 78.70(3)^\circ$, volume = $1808.6(12)$ Å³, are based upon the refinement of the XYZ-centroids of 413 reflections above $20\sigma(I)$ with $4.804^\circ < 2\theta < 39.30^\circ$. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.671. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9738 and 0.9984.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P-1$, with $Z = 2$ for the formula unit, $C_{46}H_{34}N_8O_8$. The final anisotropic full-matrix least-squares refinement on F^2 with 564 variables converged at $R1 = 7.35\%$, for the observed data and $wR2 = 13.23\%$ for all data. The goodness-of-fit was 0.759. The largest peak in the final difference electron density synthesis was 0.202 e/Å³ and the largest hole was -0.207 e/Å³ with an RMS deviation of 0.050 e/Å³. On the basis of the final model, the calculated density was 1.518 g/cm³ and $F(000)$, 860 e⁻.

CCDC- 945368 (**3b**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

^1H NMR and ^{13}C NMR spectra of 3a-3p

