Supporting information

Three-Component Reaction of 2-Oxoaldehydes, Cyclic 1,3-Dicarbonyl Compounds and 4-Aminopyridines

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Single crystal X-ray analysis

Single crystals of $6\{4,1,1\}$·$2\text{H}_2\text{O}$ ($\text{C}_{21}\text{H}_{25}\text{BrN}_4\text{O}_6$) were obtained by slow evaporation from a CDCl$_3$-DCM (~1:5) solution. A crystal, suitable for X-ray diffraction, was selected and mounted on a nylon loop on a SuperNova, Dual Source, Cu at zero diffractometer, equipped with an Atlas CCD detector using CuKα radiation ($\lambda = 1.54178$ Å) and ω scans. The crystal was kept at 100 K during data collection. The images were interpreted and integrated with the program CrysAlisPro (Agilent Technologies). Using Olex2, the structure was solved by direct methods using the ShelXS structure solution program and refined by full-matrix least-squares on $F^2$ using the ShelXL program package. Non-hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode and isotropic temperature factors fixed at 1.2 times $U$(eq) of the parent atoms.


Crystal Data for $6\{4,1,1\}$·$2\text{H}_2\text{O}$. $\text{C}_{21}\text{H}_{25}\text{BrN}_4\text{O}_6$, $M = 509.35$ g/mol, orthorhombic, space group Pbca (no. 61), $a = 12.4273(2)$ Å, $b = 16.4467(3)$ Å, $c = 21.9254(4)$ Å, $V = 4481.29(14)$ Å$^3$, $Z = 8$, $T = 100$ K, $\mu$(MoKα) = 1.880 mm$^{-1}$, $D_{calc} = 1.510$ g cm$^{-3}$, 52848 reflections measured ($6.926^\circ \leq 2\Theta \leq 59.372^\circ$), 5960 unique ($R_{int} = 0.0647$, $R_{sigma} = 0.0411$) which were used in all calculations. The final $R_1$ was 0.0397 ($I > 2\sigma(I)$) and $wR_2$ was 0.1039 (all data).

Structural features:

Compound $6\{4,1,1\}$ acquired 2 water molecules during crystallization that helps to build an H-bond network involving carbonyl groups and bromine atom.
Asymmetric unit of the crystal structure of $6\{4,1,1\}$. Thermal displacement ellipsoids are shown at the 50% probability level. Two solvent water molecules are present in the asymmetric unit.
Hydrogen bond network formed in the crystal structure of $6\{4,1,1\}$, involving water molecules, carbonyl groups and the bromine atom.
Crystal packing diagram of the crystal structure of 6\{4,1,1\}, along the crystallographic a-axis.
Hydrogen bonds are indicated.
Copies of $^1$H and $^{13}$C NMR
Comparison of $^1$H NMR of dried and stored samples.

The stored samples have higher water content.
The water signal is downfielded up to 1.7-2.4 ppm likely due to the interaction with products 6.
The crude $^1$H NMR of 8 (concentrated reaction mixture).
4-Aminopyridine fragments exchange experiments

Adduct $6\{1,1,1\}$ (0.5 mmol) was dissolved in EtOH (1.25 mL) followed by addition of 4-aminopyridine $5\{2\}$ (0.5 mmol). The resulting mixture was sealed, submerged in the oil bath preheated at 120 °C and kept with a stirring for 15 min. Upon completion of this time, an aliquot of reaction mixture was concentrated under reduced pressure and analyzed by $^1$H NMR. The establishment of the following equilibrium was observed.

![Diagram of chemical reactions and NMR spectra]
Adduct $6\{1,1,2\}$ (0.5 mmol) was dissolved in EtOH (1.25 mL) followed by addition of 4-aminopyridine $5\{1\}$ (0.5 mmol). The resulting mixture was sealed, submerged in the oil bath preheated at 120 °C and kept with a stirring for 15 min. Upon completion of this time, an aliquot of reaction mixture was concentrated under reduced pressure and analyzed by $^1$H NMR. The establishment of the following equilibrium was observed.