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### Crystal Structure of 2,8-Bis(trifluoromethyl)-4-vinylquinoline

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The X-ray crystal structure of 2,8-bis(trifluoromethyl)-4-vinylquinoline, a key intermediate in the synthesis of potent antimalarial agents, has been established. It crystallizes in the monoclinic space group  $P_{21/c}$  with cell parameters a = 16.678(2)Å, b = 17.492(7)Å, c = 8.286(4)Å,  $\beta = 97.50(2)$ , V = 2396.5(16)Å<sup>3</sup> and Z = 4. The crystal structure was refined to final values of R1 = 0.1043 and wR2 = 0.2207. An X-ray crystal structure analysis revealed that each molecule features intermolecular C-H--F hydrogen bonds and halogen halogen-type I interactions.

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Quinoline is one of the most important N-based heterocyclic aromatic compounds. Quinoline derivatives have recently attracted the attention of researchers because of their broad range of activities, and of course also for their wide applications. Thus, many synthetic or natural products that contain a quinoline core were found to be bioactive; also the versatility of quinoline and its derivatives has attracted great attention in the field of drug development, of synthetic organic chemistry as well as in the field of industrial chemistry.<sup>1-3</sup>

Following our search for antimalarial compounds, we previously described enantiopure synthetic and straightforward routes to prepare pure enantiomer aminoalcohol quinoline derivatives that showed interesting antimalarial activities.<sup>4,5</sup> We report herein on the structural characterization of the 2,8-bis(trifluoromethyl)-4-vinylquinoline, the key intermediate in the synthesis of these potent antimalarial agents (Fig. 1). The 2,8-bis(trifluoromethyl)-4-vinylquinoline was newly and easily prepared in quite good yield (87%) by a direct Suzuki-Miyaura cross-coupling reaction of 4-bromo-2,8-bis(trifluoromethyl)-quinoline with vinylboronic acid MIDA ester, performed in the presence of Pd(PPh<sub>3</sub>)<sub>2</sub>NBS as a catalyst and a 3 M aqueous solution of a sodium carbonate solution.<sup>6</sup>

Colorless crystals having dimensions of  $0.25 \times 0.10 \times 0.08 \text{ mm}^3$  suitable for X-ray diffraction analysis were obtained from a dichloromethane-methanol solution by slow evaporation of the solvent at +20°C. The molecular structure of



Fig. 1 Chemical structure of 2,8-bis(trifluoromethyl)-4-vinylquinoline.

2,8-bis(trifluoromethyl)-4-vinylquinoline is depicted in Fig. 2. Crystal and experimental data are given in Table 1.

Crystallographic data of this key intermediate compound were collected at 293 K on a Bruker Kappa CCD diffractometer using monochromatic Mo- $K\alpha$  radiation ( $\lambda = 0.71073$  Å). The collected data were reduced using SAINT software (SAINT, Bruker AXS Inc., Madison, WI, USA), and all reflections were used for unit-cell refinement. The crystal structure was solved by direct methods and successive Fourier difference syntheses with the SHELXS program.7 Refinement of the crystal structure was performed on  $F^2$  by weighted anisotropic full-matrix leastsquares methods using the SHELXL program.7 An absorption correction was performed by semi-empirical methods using the SADABS program.7 All parts of program were used within the OLEX2 package.8 All non-H atoms were refined anisotropically, and the positions of the H atoms were deduced from the coordinates of the non-H atoms to which they are linked, confirmed by Fourier synthesis and treated according to the riding model during refinement. H atoms were included for structure factor calculations, but not refined.

The title compound crystallizes in the monoclinic  $P2_1/c$  space group, and the asymmetric unit is constituted by two independent molecules of 2,8-bis(trifluoromethyl)-4-vinylquinoline, denoted



Fig. 2 Asymmetric unit ORTEP view of the crystal structure of the title compound (molecules A and B) with our numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. Distorted CF<sub>3</sub> molecules have been omitted for clarity.

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 Table 1
 Crystal and experimental data for the title compound

Chemical formula: C<sub>26</sub>H<sub>14</sub>F<sub>12</sub>N<sub>2</sub> Formula weight: 582.39 T = 293(2)K Crystal system: monoclinic Space group:  $P2_1/c$ a = 16.678(2)Å b = 17.492(7)Å c = 8.286(4)Å  $\beta = 97.50(2)$ V = 2396.5(16)Å<sup>3</sup> Z = 4 $D_x = 1.614 \text{ Mg/m}^3$ Radiation: Mo  $K\alpha$  ( $\lambda = 0.71073$  Å) F(0,0,0) = 1168.0Crystal size =  $0.25 \times 0.10 \times 0.08$  mm<sup>3</sup> No. of reflections collected = 15792 No. of independent reflections = 4195No. of reflections used  $[I > 2\sigma(I)] = 1895$  $\theta$  range for data collection: 5.27 to 50.05° Data/Restraints/Parameters = 4195/216/417 Goodness-of-fit = 1.215*R* indices  $[I > 2\sigma(I)]$ : *R*1 = 0.1043, *wR*2 = 0.1891 *R* indices (all data): R1 = 0.2051, wR2 = 0.2207 $(\Delta/\sigma)_{\rm max} = 0.000$  $(\Delta \rho)_{\rm max} = 0.550 \text{ Å}^{-3}$  $(\Delta \rho)_{\rm min} = -0.275 \text{ Å}^{-3}$ Measurement: Bruker Kappa CCD diffractometer Structure determination: SHELXS7 Refinement: SHELXL7 CCDC deposition number: 1563782

by A and B (Fig. 2). The quinoline moieties are almost planar, and the maximum deviation from planarity have been found for C(5) lying -0.017(5)Å and for C(15) lying -0.020(4)Å from planes defined by the heterocyclic systems. Vinyl C(11)-C(12)and C(24)-C(25) double bonds were respectively noticed at 1.282(8) and 1.264(8)Å, which is a bit shorter, but in the same range as those observed in vinyl substituted derivatives.9 The vinyl group is probably slightly disordered on several close positions, and thus explaining the high atomic displacement parameters of C(12) and C(25) and the slightly shorter doublebond length than expected. The C-C distances within the sixmembered benzene rings are in the range of 1.296 to 1.469 Å consistent with the aromatic character of the ring system. The length of the C(4)-C(11) and C(17)-C(24) coupled bonds are 1.409(8) and 1.426(8)Å, whereas the N(1)-C(2) and N(1)-C(6), then N(2)-C(15) and N(2)-C(19), bond lengths were found to be 1.366(7), 1.306(7), 1.358(7) and 1.324(6)Å, respectively, suggesting delocalization in the quinoline rings. The CF<sub>3</sub> moieties bonded to the pyridine ring are distorted, also their occupation factors were refined separately, leading to a 50/50 and a 79/21 ratio of for molecules A and B, respectively. The C-F bonds were noticed in the range of 1.240 to 1.327 Å, as typically observed for C-F<sub>3</sub> bonds.<sup>9</sup> The interplanar dihedral angle between the quinoline rings and the vinyl substituent in molecules A and B were both observed at 23.02(9)° and 21.16(8)°, respectively. Molecules are linked by C-HF hydrogen bonds, C-FF type I or quasi type I halogen-halogen interactions10 and  $\pi$ - $\pi$  interactions to form a tridimensional network (Fig. 3). Interactions also involved one fluorine atom of the trifluoromethyl group and vinyl substituent with a short contact C - F =3.147(2)Å that link molecules A and B together. Pertinent short-contact distances are given in Table S1. Molecules A and B are quasi identical, since an overlay of both molecules gave a RMSD (excluding hydrogens and distorted fluorines) of only



Fig. 3 View of the crystal packing of the title compound, showing the most important interactions. Distorted  $CF_3$  and hydrogen atoms have been omitted for clarity when not involved in an any intermolecular interaction.

0.025 Å. However, the intermolecular interactions significantly differ between both molecules. Molecule A presents slightly weaker interactions than molecule B, and differs concerning the  $\pi$ - $\pi$  interactions. While molecule B presents  $\pi$ - $\pi$  interactions on both sides of the quinoline plane between the pyridine ring and the benzene ring (centroid-centroid distance = 3.695 Å), molecule A presents  $\pi$ - $\pi$  interactions only on one side between two benzene rings and on the other side between the ethylene group and a pyridine ring (centroid-centroid distance = 3.693 and 3.826 Å, respectively).

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#### **Supporting Information**

A CIF format file and Table S1. These material is available free of charge on the Web at http://www.jsac.or.jp/xraystruct/.

#### References

- 1. S. M. Prajapati, K. D. Patel, R. H. Vekariya, S. N. Panchal, and H. D. Patel, *RSC Adv.*, **2014**, *4*, 24463.
- P.-Y. Chung, Z.-X. Bian, H.-Y. Pun, D. Chan, A. Sun-Chi Chan, C.-H. Chui, J. Cheuk-On Tang, and K.-H. Lam, *Future Med. Chem.*, 2015, 7, 947.
- 3. S. M. A. Hussaini, Expert Opin. Ther. Pat., 2016, 26, 1201.
- A. Jonet, A. Dassonville-Klimpt, S. Da Nascimento, J.-M. Leger, J. Guillon, and P. Sonnet, *Tetrahedron: Asymmetry*, 2011, 22, 138.
- 5. G. Bentzinger, W. De Souza, C. Mullié, P. Agnamey, A. Dassonville-Klimpt, and P. Sonnet, *Tetrahedron: Asymmetry*, **2016**, *27*, 1.
- L. Ronga, M. Del Favero, A. Cohen, C. Soum, P. Le Pape, S. Savrimoutou, N. Pinaud, C. Mullié, S. Daulouede, P. Vincendeau, N. Farvacques, P. Agnamey, F. Pagniez, S. Hutter, N. Azas, P. Sonnet, and J. Guillon, *Eur. J. Med. Chem.*, 2014, 81, 378.
- 7. G. M. Sheldrick, Acta Crystallogr. Sect. A, 2008, 64, 112.
- 8. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard, and H. Puschmann, J. Appl. Cryst., 2009, 42, 339.
- F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, J. Chem. Soc. Perkin Trans. II, 1987, S1.
- G. Cavallo, P. Metrangolo, R. Milani, T. Pilati, A. Priimagi, G. Resnati, and G. Terraneo, *Chem. Rev.*, **2016**, *116*, 2478.