

Unveiling the molecular conformation of 2-(2-pyridyl)benzo[b]thiophene using jet-cooled rotational spectroscopy

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Sulfur-containing heterocycles hoard a major scientific interest for its key role in natural and pharmaceutical products [1,2]. One of these compounds is 2-(2-pyridyl)benzo[b]thiophene, a heterobiarylic molecule whose structural insights are addressed here using computational methods and rotational spectroscopy.

Theoretical calculations have included density functional predictions (B3LYP-D3 and B2PLYP-D3) for the title molecule and its monohydrate, using Ahlrichs (def2-TZVP) and Pople basis sets (6-311G(d)). The investigation of the rotational spectrum used chirped-pulse broadband Fourier transform microwave spectroscopy in a supersonic jet expansion, operating in the 2-8 GHz region.

Two conformers were detected in the rotational spectrum. The *cis*-locked geometry has emerged as preferential by ca. 2.25 kJ mol⁻¹, although transitions associated with the *trans* species have been also detected. The rotational constants and the nuclear quadrupole coupling constants determined experimentally present a satisfactory agreement with the computational predictions. Both conformers are effectively planar, with a small inertial defect caused by low-frequency vibrations. Finally, the non-covalent interactions have been rationalized using the non-covalent interactions index and natural bond orbitals calculations. Both methods confirm the role of the N⋯S interaction to drive the molecular orientation.

[1] R.S. Keri, K. Chand, S. Budagumpi, S. Balappa Somappa, S.A. Patil, B.M. Nagaraja, An overview of benzo [b] thiophene-based medicinal chemistry, *Eur J Med Chem.* 138 (2017) 1002–1033. <https://doi.org/10.1016/j.ejmech.2017.07.038>.

[2] B.R. Beno, K.-S. Yeung, M.D. Bartberger, L.D. Pennington, N.A. Meanwell, A Survey of the Role of Noncovalent Sulfur Interactions in Drug Design, *J Med Chem.* 58 (2015) 4383–4438. <https://doi.org/10.1021/jm501853m>.

