Supporting Information for

A mechanochemical approach to access the proline–proline diketopiperazine framework

Nicolas Pétry1, Hafid Benakki1,2, Eric Clot3, Pascal Retailleau4, Farhate Guenoun2, Fatima Asserar2, Chakib Sekkat2, Thomas-Xavier Métro1, Jean Martinez1 and Frédéric Lamaty1

Address: 1Institut des Biomolécules Max Mousseron (IBMM), UMR 5247, CNRS, Université de Montpellier, ENSCM, Campus Triolet, Place Eugène Bataillon, 34095 Montpellier Cedex 5, France, 2Laboratory of Chemistry Biology Applied to the Environment, Faculty of Sciences, Moulay Ismail University BP: 11201 Zitoune Meknès, Morocco, 3Institut Charles Gerhardt, UMR 5253 CNRS-UM-ENSCM, Université de Montpellier, Place Eugène Bataillon, cc 1501, 34095 Montpellier Cedex 5, France and 4Institut de Chimie des Substances Naturelles, CNRS UPR 2301, Université Paris-Saclay, 1 Avenue de la Terrasse, 91198 Gif-sur-Yvette, France

Email: Thomas-Xavier Métro - thomas-xavier.metro@umontpellier.fr; Frédéric Lamaty - frederic.lamaty@umontpellier.fr

*Corresponding author

Crystallographic data
Diffraction data were collected at room temperature on a RIGAKU XtaLabPro diffractometer equipped with a Mo microfocus sealed tube generator coupled to a double-bounce confocal Max-Flux® multilayer optic and a HPAD PILATUS3 R 200K detector for compound 10 and 15a, or on a Rigaku MM007 HF copper rotating-anode generator equipped with Osmonic confocal optics and a rapid II Curved Image Plate for compound 19. Appropriate versions of the CrystalClear21 were used according to the diffractometer to record and process the data. The structures were solved by new intrinsic phasing methods (SHELXL2)2 and refined by full-matrix least-squares on F2 values (SHELXL)3. All heavy atoms were refined anisotropically. Hydrogen atoms were localized in difference electron density maps, but were refined isotropically with appropriate riding models. ORTEP-III4 was used for structure presentation.

The meso form of the structure of compound 10 is confirmed around the crystallographic centre of inversion in the middle of the C1 - C1A bond, as previously shown by Feng and coll (2010)5, CSD RefCode: WADCAH. Disorder is found in compound 15a: the methyl group displays two sets of methyl hydrogens that were refined with AFIX 123 and major part of occupancy refined to 0.58 (4) for C12, as well as the outer 5-membered ring that adopts in majority (occupancy factor of 0.65(2)) an envelope conformation on C2 whereas the minor conformation is similar to that of the opposite five-membered ring, whose closest pucker descriptor6 is a twist on C3B–C4 (C7–C8, respectively). The absolute configuration (C1:S, C6:S and C9:R) is also determined based on significant Flack parameter7 (–0.1(2)) and Bijvoet analysis using likelihood methods8 (probability that the structure is inverted is only 0.2%) thanks to highly redundant good quality data albeit measured with a molybdenum radiation. The same level of confidence can be applied to the compound 19, which accommodates a two-fold rotation axis crossing the central diketopiperazine moiety orthogonally. The stereocentres C1 and C4 and those generated by the symmetry operation 1-x, y, 2-z are S and R respectively.

The crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. Copies of the data can be obtained free of charge on application to CCDC, e-mail: deposit@ccdc.cam.ac.uk.

X-ray data of compound 10: C₈H₁₂Br₂O₄, M = 332.0 g/mol, monoclinic system, space group P2₁/c, a = 4.5421(4), b = 12.143(1), c = 10.5679(9) Å, β = 90.227(11) (9)°, Z = 2, V = 582.87(9) Å³, Dc = 1.892 g·cm⁻³, μ(Mo Kα) = 6.941 mm⁻¹, T = 293 K, crystal dimensions of 0.42 × 0.07 × 0.05 mm. The structure converged to the final R = 0.0431 and Rw = 0.0522 using 1331 independent reflections (θmax = 27.56°). CCDC registration number 1552540.
Figure S6. ORTEP projection of compound 10. Displacement ellipsoids are drawn at the 50% probability level. Atoms labeled with the suffixes a are generated by the symmetry operation (1/2 - x, 3/2 - y, 1 - z).

X-ray data of compound 15_a: C_{12}H_{16}N_{2}O_{4}, M = 252.27 g/mol, orthohombic system, space group P2_12_12_1, a = 5.9495(4), b = 9.7200(7), c = 21.3731(15) Å, Z = 4, V = 1215.21(15) Å³, D_c = 1.379 g·cm⁻³, µ(Mo Kα) = 0.104 mm⁻¹, T = 293 K, crystal dimensions of 0.31 × 0.08 × 0.06 mm. The structure converged to the final R = 0.0346 and Rw = 0.0925 using 2765 independent reflections (θ_{max} = 25.24°). CCDC registration number 1552541.
Figure S7. ORTEP projection of compound 15a, ellipsoid probability 50%. No disorder is shown.

X-ray data of compound 19: C14H18N2O6, $M = 310.30$ g/mol, monoclinic system, space group $C2$, $a = 12.5371(10)$, $b = 12.143(5)$, $c = 10.5679(7)$ Å, $\beta = 105.615(9)^\circ$, $Z = 2$, $V = 737.75(10)$ Å³, $D_C = 1.397$ g·cm⁻³, $\mu$(Mo Kα) = 0.933 mm⁻¹, $T = 293$ K, crystal dimensions of $0.31 \times 0.18 \times 0.09$ mm. The structure converged to the final $R = 0.0462$ and $R_w = 0.0968$ using 1339 independent reflections ($\theta_{\text{max}} = 67.68^\circ$). CCDC registration number 1552542.
Figure S8. ORTEP projection of compound 19, ellipsoid probability 50%

References for crystallographic data


