Impact of Polymorphism on Mechanical Properties of Molecular Crystals: A study of *p*-Amino and *p*-Nitro Benzoic Acid with Nanoindentation.

Benjamin P. A. Gabriele[a], Craig J. Williams[b], Matthias E. Lauer[c], Brian Derby[b], Aurora J. Cruz-Cabeza[a]*

[a] School of Chemical Engineering and Analytical Science, University of Manchester, UK.
[b] School of Materials, University of Manchester, UK.
[c] Roche Innovation Center Basel, Basel, Switzerland

*Email: aurora.cruzcabeza@manchester.ac.uk

Abstract: This Electronic Supplementary Information (ESI) includes the results of single crystal x-ray diffraction measurements, similarities in crystal packing of polymorphs of *p*NBA, the trapezoid load functions used for the nanoindentation experiments, images of the indents and the periodic bond chains of the two pairs of polymorphs of *p*NBA and *p*ABA.

S1. Experimental Methods

Single Crystal X-ray Diffraction. Single crystals of *p*NBA (forms I and II) and *p*ABA (α and β forms) were mounted on a spindle using a thick microscope oil and their crystal lattice was determine at room temperature using a single crystal x-ray diffractometer (XCalibur-2, Oxford) equipped with a MoKα X-ray source (λ = 0.71073Å). Using the software CrysAlisPro[1] (version 171.40.14d, Rigaku Oxford Diffraction), from the X-ray measurements the unit cells of each single crystal were determined and verified to match the CSD refcode associated, so that to confirm the polymorphic form.

Nanoindentation. Experiments were carried out on 7 to 10 single crystals per molecule studied (9 indents per crystal) using a Hysitron Ti950 Triboindenter (Hysitron/Bruker) equipped with a diamond Berkovich probe. Indentations were conducted in either load-control or displacement-control mode using a trapezoid load function. We first investigated the optimal maximum displacement/load as defined in a previous work, so the modulus and hardness measured do not vary for further increase of decrease of P_{MAX} or h_{MAX}.[2] The trapezoid load functions used were hence adapted for each compound studied.

Imaging. Indents were imaged either in-situ, with the same probe used to carry out the indents (in-situ scanning probe microscopy in contact mode, 2 μN) or via Atomic Force Microscopy (AFM, Multimode 8, Bruker) using Peak Force QNM in air and with a TESP-V2 probe (k = 42 N/m).

S2. Single crystal X-ray data

Comparison between experimental ("Experim.") results of single crystal x-ray diffraction data and crystallographic data from associated CSD refcode is hereafter shown:

	***p*NBA-I** **Experim. / NBZOAC03**[3]	***p*NBA-II** **Experim. / NBZOAC14**[4]	**α-*p*ABA** **Experim. / AMBNAC06**[5]	**α-*p*ABA** **Experim. / AMBNAC04**[6]
SG	$A2_1/a$	$P2_1/c$	$P2_1/n$	$P2_1/n$
a (Å)	12.959 / 12.918	5.482 / 5.473	18.569 / 18.571	6.281 / 6.278
b (Å)	5.039 / 5.042	5.222 / 5.209	3.840 / 3.843	8.592 / 8.583
c (Å)	21.330 / 21.298	24.740 / 24.729	18.670 / 18.632	12.365 / 12.365
α (°)	90	90	90	90
β (°)	96.67 / 96.66	95.57 / 95.41	93.66 / 93.67	100.15 / 100.13
γ (°)	90	90	90	90
Z; Z'	8; 1	4; 1	8; 2	4; 1
V ($Å^3$)	1384.0 / 1377.8	705.0 / 701.0	1328.4 / 1327.1	656.9 / 655.9

S3. Crystal packing similarities

The Crystal Packing Similarity module (derived from the module COMPACK), integrated in the software Mercury, was used to compare and assess similarities between crystal packing of *p*NBA-I and *p*NBA-II. Layers in common stack in both cases along [101], as shown in Figure S3. No common packing/layers were observed between α-*p*ABA and β-*p*ABA.

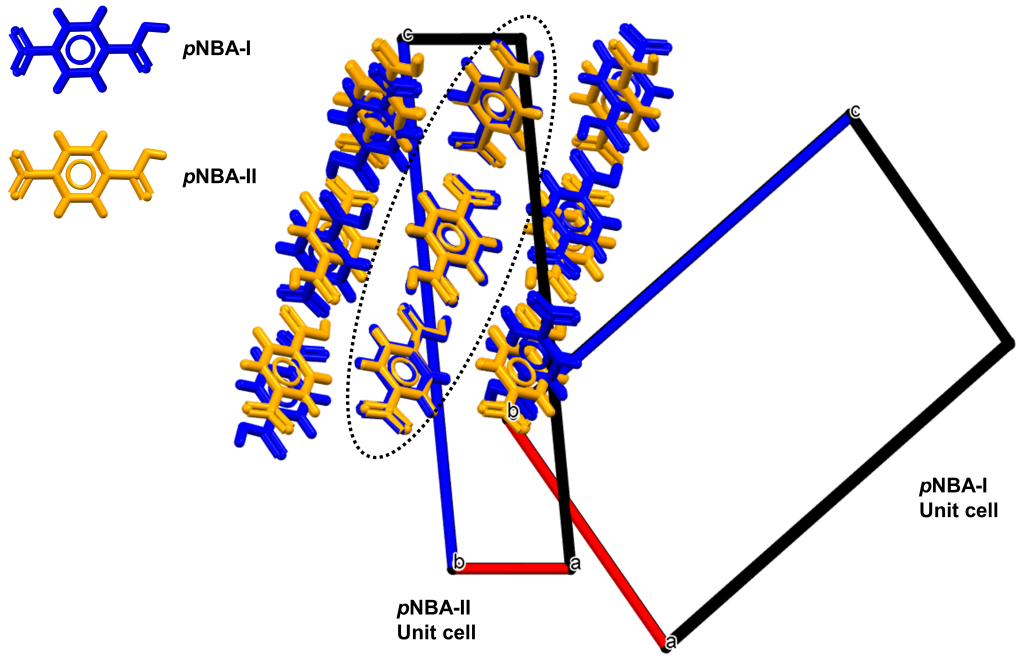
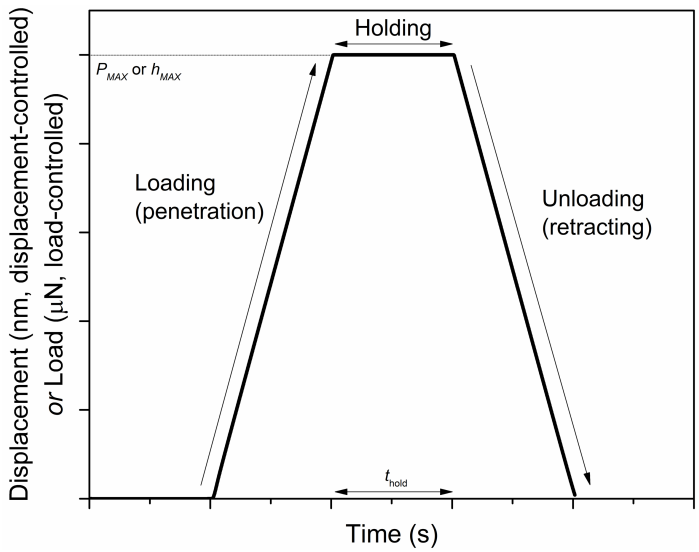


Figure S3: Comparison of crystal packing of pNBA-I (molecules in blue) and pNBA-II (molecules in yellow).

S4. Nanoindentation – Load function



Compound	Mode	P_{MAX} (µN) / h_{MAX} (nm)	t_{hold} (s)
*p*ABA [α] & [β]	Load-controlled	5000 µN	5
*p*NBA [I] & [II]	Displacement-controlled	425 nm	2

Figure S4: The trapezoid load function used on *p*ABA and *p*NBA is presented here along with the different parameters, namely the mode used (load-controlled or displacement-controlled), the maximum load P_{MAX} or maximum displacement h_{MAX} used and the holding time used.

S5. Nanoindentation – Images

Images of indents on α-*p*ABA and β-*p*ABA were acquired via AFM while images on indents on both forms of *p*NBA were acquired in-situ, using the Berkovich tip used for the indentation as probe, in contact mode and with a force of 2µN. Images are shown in Figure S5.

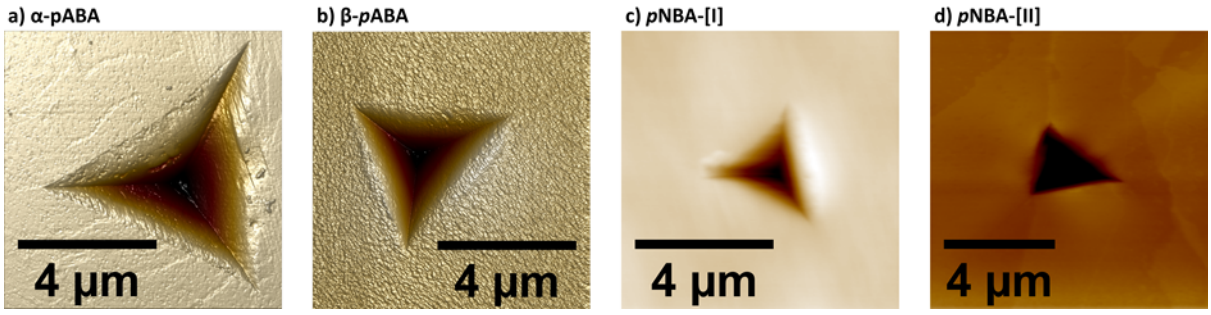


Figure S5: AFM height images of α-*p*ABA (a) and β-*p*ABA (b) *p*ABA, and *in-situ* SPM images in contact mode (2µN) of (c) *p*NBA-[I] and (d) *p*NBA-[II].

S6. Lattice Energies, Cohesive Energy Densities

Table S6: E_R and H data (average ± stdv) measured by nanoindentation on *p*NBA forms I and II and *p*ABA forms α and β. Space Group (SG) and *hkl* indices of the indented face are also given, along with the calculated lattice energies with CompassII (U_{Latt}) and cohesive energy density (CED).

Compound	SG	Indented Face	Nanoindentation E_R ± stdv (GPa)	Nanoindentation H ± stdv (MPa)	U_{LATT} (kJ/mol)	CED (MPa)
*p*ABA [α]	$P2_1/n$	(200)	7.88 ± 0.28	221 ± 17	-104.3	1045
*p*ABA [β]	$P2_1/n$	(10-1)	12.50 ± 0.35	512 ± 25	-119.5	1210
*p*NBA [I]	*A*2/a	(002)	10.1 ± 0.53	322 ± 22	-111.6	1077
*p*NBA [II]	$P2_1/c$	(002)	6.46 ± 0.28	182 ± 10	-106.3	1006

References

(1) CrysAlis PRO, Version 171.40.14d, Oxford Diffraction /Agilent Technologies UK Ltd, Yarnton, England. 2018.

(2) Gabriele, B. P. A.; Williams, C. J.; Lauer, M. E.; Derby, B.; Cruz-Cabeza, A. J. Nanoindentation of Molecular Crystals: Lessons Learned from Aspirin. *Cryst. Growth Des.* **2020**, *20*, 5956–5966.

(3) Colapietro, M.; Domenicano, A. Structural Studies of Benzene Derivatives. II. Refinement of the Crystal Structure of p-Nitrobenzoic Acid. *Acta Crystallogr. Sect. B Struct. Crystallogr. Cryst. Chem.* **1977**, *33*, 2240–2243.

(4) Light, M. E. CCDC 1476879. *CSD Commun.* **2016**.

(5) Athimoolam, S.; Natarajan, S. 4-Carboxy-Anilinium (2R,3R)-Tartrate and a Redetermination of the α-Polymorph of 4-Amino-Benzoic Acid. *Acta Crystallogr. Sect. C Cryst. Struct. Commun.* **2007**, *63*, 514–517.

(6) Gracin, S.; Fischer, A. Redetermination of the β-Polymorph of p-Aminobenzoic Acid. *Acta Crystallogr. Sect. E Struct. Reports Online* **2005**, *61*.