

# Mechanically Induced *Cis-to-Trans* Isomerization of Carbon-Carbon Double Bond Using Atomic Force Microscopy

## Supplementary Information

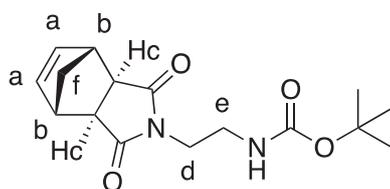
by Milad Radiom, Phally Kong, Plinio Maroni, Mark Schäfer, Andreas F.M. Kilbinger and Michal Borkovec

### Materials and Characterization

All commercially available reagents and solvents (Sigma Aldrich, Acros, ABCR and Fluorochem) were used without further purification.  $\text{CDCl}_3$  was purchased from Cambridge Isotope Laboratories. Reactions were monitored by TLC, Merck silica gel 60F254 plates. Detection was performed by UV light,  $\text{KMnO}_4$ , ninhydrin or  $\text{I}_2$  staining reagents. Purifications were performed by flash chromatography on silica gel (technical grade, pore size 60 Å, 230-400 mesh, 40-63  $\mu\text{m}$  particle size).

Standard nuclear magnetic resonance spectra as well as two-dimensional spectra were recorded at 300 MHz ( $^1\text{H}$  NMR) and 75 MHz ( $^{13}\text{C}$  NMR) on a Bruker Avance III 300. All NMR signals were referenced internally to residual solvent signals. Relative molecular weights and molecular weight distributions were measured by gel permeation chromatography (GPC) equipped with a Viscotek GPCmax VE2001 GPC Solvent/Sample Module, Viscotek UV-Detector 2600, Viscotek VE3580 RI-Detector, and two Viscotek T6000 M columns (7.8  $\times$  300 mm,  $10^3$ - $10^7$  g/mol each). All measurements were carried out at room temperature using THF as the eluent with a flow rate of 1 mL/min. The system was calibrated with polystyrene standards in a range from  $10^3$  to  $3 \times 10^6$  g/mol. High resolution mass spectrometry (HRMS) was performed by Bruker FTMS 4.7T BioAPEX II ESI-MS.

### Synthesis of monomer 1, tert-butyl (2-((3aR,4R,7S,7aS)-1,3-dioxo-1,3,3a,4,7,7a-hexahydro-2H-4,7-methanoisoindol-2-yl)ethyl)carbamate



5-Norbornene-2,3-dicarboxylic anhydride (2.2 g, 13 mmol) was added dropwise to a flask containing vigorously stirred ethylenediamine (7.2 mL, 107 mmol) in toluene (45 mL) at room temperature and connected to a Claisen condenser. The reaction temperature was raised to 110°C for 8h. Toluene and ethylenediamine were then removed by distillation. Purification by column chromatography on silica gel DMC/MeOH 9:1 gave *exo*-N-(2-aminoethyl)-5-norbornene-2,3-dicarboximide as a white solid (1.57 g, 7.6 mmol) with 57% yield. The analytical data of this amine intermediate were in accordance with reported characterization.<sup>1</sup>

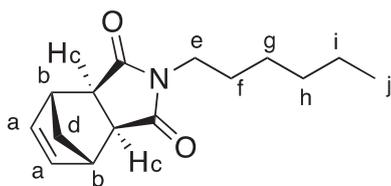
To a solution of the above amine (1.4 g, 6.8 mmol) in DCM (45 ml) di-tert-butyl-dicarbonate (2.97 g, 13.6 mmol) and triethylamine (0.88 g, 1.22 ml, 8.7 mmol) were added. The reaction mixture was allowed to stir overnight. The reaction mixture was then washed with 10% aqueous citric acid solution (130 ml) and the organic layer separated, dried over MgSO<sub>4</sub>, filtered and the solvent was removed under reduced pressure. This crude product was subject to column chromatography using 9:0.25 DCM:MeOH as eluent. Fractions containing the desired product were combined and the solvent removed under reduced pressure to afford monomer **1** as a white powder (0.81 g, 3.26 mmol) with 39 % yield.<sup>2,3</sup>

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): δ (ppm) = 6.27 (t, <sup>3</sup>J = 1.72 Hz, 2Ha), 4.77 (s, 1H, NHBOC), 3.61 (t, <sup>3</sup>J = 5.50 Hz, 2Hd), 3.33 (m, 2He), 3.26 (t, <sup>3</sup>J = 1.5 Hz, 2Hb), 2.68 (d, <sup>3</sup>J = 1.19 Hz, 2Hc), 1.50 (d, <sup>3</sup>J = 9.84 Hz, 1Hf), 1.40 (s, 9H, tBu), 1.24 (d, <sup>3</sup>J = 9.84 Hz, 1Hf').

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ (ppm) = 178.31 (CO); 160 (NHC=O); 137.95 (C=C); 79.55 (O-C(CH<sub>3</sub>)<sub>3</sub>); 48.03 (CO-CH); 45.29 (=CH-CH); 42.98 (CH<sub>2</sub>-bridge); 39.29 (CO-N-CH<sub>2</sub>); 38.58 (CH<sub>2</sub>NHCO); 28.46 (tBu).

HRMS: mass calculated 329.1471783, mass found 329.1469080.

#### Synthesis of monomer **2**, (3aR,4R,7S,7aS)-2-hexyl-3a,4,7,7a-tetrahydro-1H-4,7-methanoisindole-1,3(2H)-dione



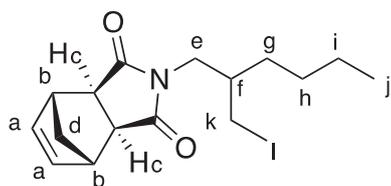
Monomer **2** was synthesized following the general procedure reported for monomer **4** (see below).<sup>4</sup>

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): δ (ppm) = 6.25 (t, <sup>3</sup>J = 1.80 Hz, 2Ha), 3.41 (t, <sup>3</sup>J = 7.47 Hz, 2He), 3.23 (quin, <sup>3</sup>J = 1.69 Hz, 2Hb), 2.63 (d, <sup>3</sup>J = 1.32 Hz, 2Hc), 1.66 (quin, <sup>3</sup>J = 6.55 Hz, 1Hf), 1.47 (dquin, <sup>3</sup>J = 9.88, 1.57 Hz, 1Hd'), 1.29-1.22 (m, 6Hg,h,i), 1.19 (dquin, 9.80, 1.40, 1Hd''), 0.83 (t, <sup>3</sup>J = 6.68 Hz, 3Hj).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ (ppm) = 178.11 (2(C=O)); 137.89 (2Ca); 47.85 (2Cc); 45.23 (2Cb); 42.77 (1Cd); 38.80 (1Ce); 31.36 (Ch); 27.78 (Cf); 26.67 (Cg); 22.52 (Ci); 14.03 (Cj).

HRMS: mass calculated 270.1464500, mass found 270.1465230.

#### Synthesis of monomer **4**, (3aR,4R,7S,7aS)-2-(2-ethylhexyl)-3a,4,7,7a-tetrahydro-1H-4,7-methanoisindole-1,3(2H)-dione



Endo-carbic anhydride (500 g, 3.05 mol) was heated to 180°C for 2h and recrystallized from acetone several times to obtain the pure exo-carbic anhydride (101,9 g, 20% yield).

To a round bottom flask connected to a Claisen condenser containing exo-carbic anhydride (32.83 g, 200 mmol), toluene (200 mL) was added until complete dissolution of the solid. Then 2-ethylhexylamine (26.88 mg, 208 mmol) was added and the reaction mixture was heated at 110°C. After 2h of stirring at 110°C the solution was heated to 150°C to remove toluene by distillation. The crude product was then purified by column silica gel chromatography, hexane/EtOAc 9:1 (Rf 0.25), to afford the monomer (52.77 g, 0.192 mol) as a yellow oil with 96% yield.<sup>4</sup>

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): δ (ppm) = 6.24 (t, <sup>3</sup>J = 1.81 Hz, 2Ha), 3.32 (d, <sup>3</sup>J = 7.16 Hz, 2He), 3.23 (t, <sup>3</sup>J = 1.64 Hz, 2Hb), 2.63 (d, <sup>3</sup>J = 1.18 Hz, 2Hc), 1.66 (sep, <sup>3</sup>J = 6.12 Hz, 1Hf), 1.47 (dquin, <sup>3</sup>J = 9.99, 1.47 Hz, 1Hd'), 1.31-1.1 (m, 9Hg,h,i,k,d''), 0.89-0.78 (m, 6Hj,l).

<sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ (ppm) = 178.41 (C=O); 137.87 (2Ca); 47.82 (2Cc); 45.21 (2Cb); 42.83 (1Ce); 42.56 (1Cf); 37.79 (Cg); 30.56 (Ci); 28.45 (Cj); 23.96 (Cm); 23.02 (Ck), 14.10 (Cl); 10.40 (Cn).

HRMS: mass calculated 298.1777501, mass found 298.1776420.

### Synthesis of polymers **3** and **P1**

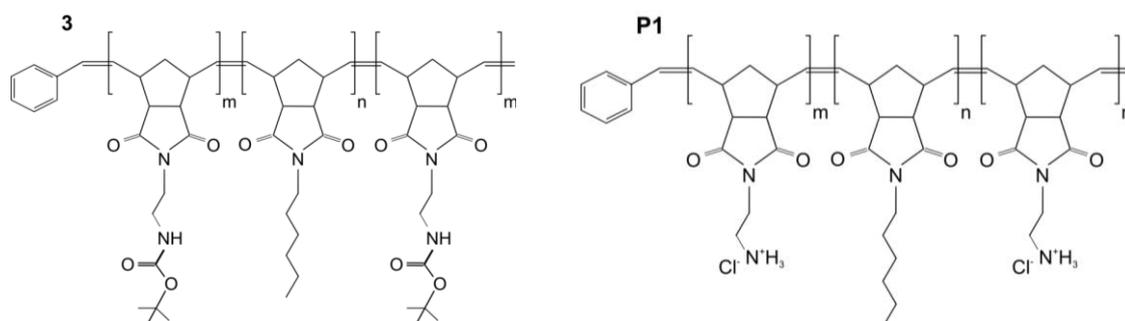


Figure S1: Polymers **3** and **P1** synthesized in this work with  $m \cong 11$ ,  $n \cong 544$ .

An ABA triblock copolymer that contains carbon-carbon double bond in the backbone was synthesized from N-hexylnorbornen-5,6-dicarboxylicimide monomer **2** and N-BOC-ethylenediamine-exo-norbornen-5,6-dicarboxylicimide monomer **1** in the following manner: a sealed Schlenk flask containing monomer **1** (32 mg) was placed under vacuum and purged with argon three times before degassed dichloromethane (2 mL) was added via a syringe. The polymerization was initiated by quickly adding a solution of the appropriate amount of Grubbs' third generation catalyst in degassed dichloromethane. The reaction mixture was stirred for 45 min at room temperature. After the complete conversion of **1**, a solution of monomer **2** (936 mg) in degassed dichloromethane (8 mL) was added quickly via a syringe, and the mixture was stirred until no residual monomer was left (monitored by GPC). Then a solution of monomer **1** (32 mg) in degassed dichloromethane (2 mL) was quickly added. After the complete conversion of **1** (monitored by GPC) the polymerization was termi-

nated using ethyl vinyl ether. The polymer was then redissolved in dichloromethane and precipitated twice into methanol. The block copolymer was dried under vacuum to give **3** (820 mg) with 82 % yield.<sup>1</sup>

To a solution of **3** (85 mg) in DCM, an aqueous solution of HCl (37%) was added and the reaction mixture was allowed to stir for 12 h. Then the solvent was removed under vacuum and the solid was redissolved in DCM and then precipitated in methanol and dried under vacuum to give **P1** (68.5 mg) with 77 % yield.

Structures of polymers **3** and **P1** are shown in Figure S1. The number average molecular weight of block polymer **3** is  $M_n = 4300$  g/mol with dispersity of  $D = 1.2$ . For diblock polymer **3**,  $M_n = 170000$  g/mol and  $D = 1.2$ . For triblock polymer **3**,  $M_n = 145000$  g/mol and  $D = 1.6$ . For polymer **P1**,  $M_n = 145000$  g/mol and  $D = 1.6$ . The apparent loss of molecular weight is most likely due to a reduced hydrodynamic radius caused by aggregation (hydrogen bonds) of the BOC-amine terminal blocks.

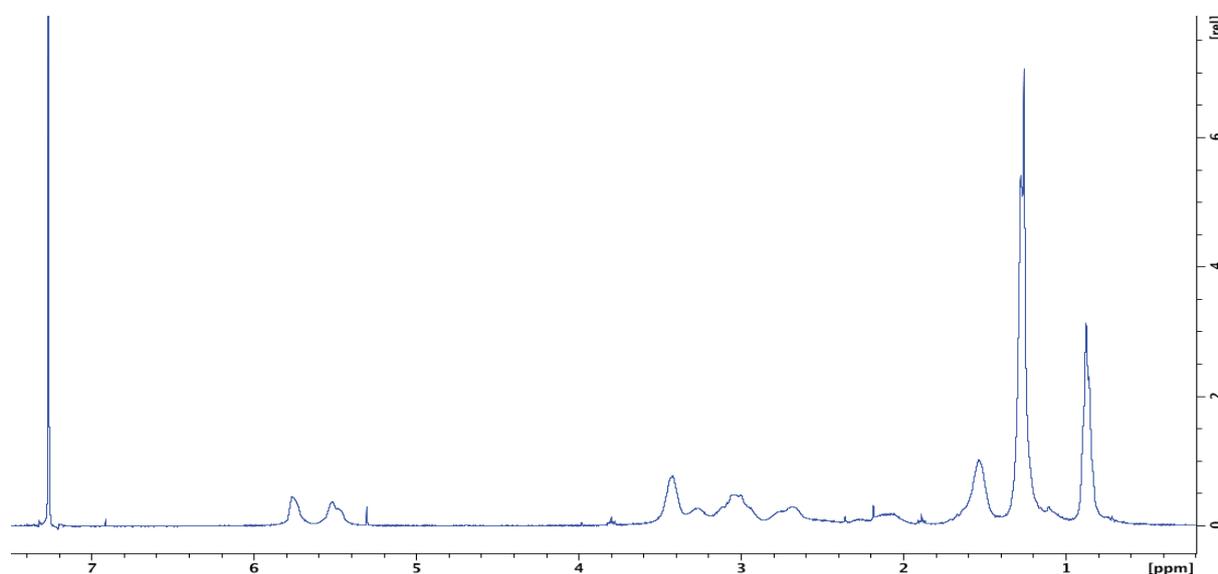
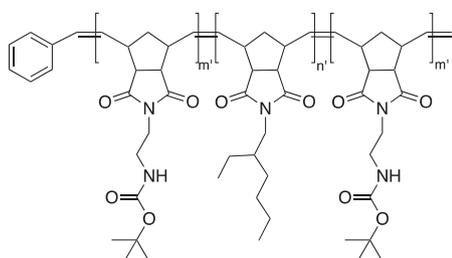


Figure S2: <sup>1</sup>H-NMR spectrum (300 MHz, CDCl<sub>3</sub>) of the “BOC deprotected” polymer **3**.

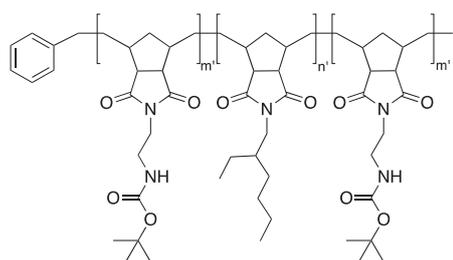
### Synthesis of polymer **5** with $m' \cong 8$ , $n' \cong 293$



A sealed Schlenk flask containing monomer **1** (25.5 mg) was placed under vacuum and purged with argon three times before degassed dichloromethane (2 mL) was added via a syringe. The polymerization was initiated by quickly adding a solution of the appropriate amount of first generation Grubbs catalyst (20.5 mg) in degassed dichloromethane (2 mL). Then the S4

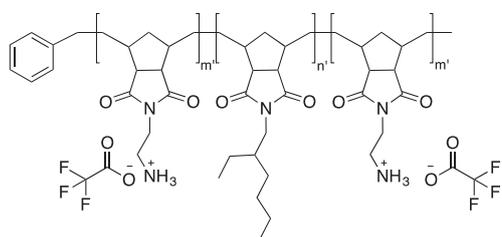
reaction mixture was stirred for 45 min at room temperature. After the complete conversion of **1** (monitored by GPC), a solution of **4** (949 mg) in degassed dichloromethane (8 mL) was added quickly via a syringe, and the mixture was stirred until no residual monomer was left (determined via GPC). Then a solution of **1** (26 mg) in degassed dichloromethane (2 mL) was added quickly. After the complete conversion of **1** (monitored by GPC) the polymerization was terminated with ethyl vinyl ether (2 mL) before precipitating **5** in methanol. The polymer was then redissolved in dichloromethane and precipitated in MeOH twice. The block copolymer was dried under vacuum to give **5** (0.879 g) with 88% yield. The number average molecular weight of block polymer **5** is  $M_n = 3000$  g/mol with dispersity of  $D = 1.3$ . For diblock polymer **5**,  $M_n = 73000$  g/mol and  $D = 1.3$ . For triblock polymer **5**,  $M_n = 85000$  g/mol and  $D = 1.3$ .<sup>1</sup>

### Synthesis of polymer 6



Polymer **5** (358 mg) was added to the reaction vessel and was evacuated and backfilled with argon gas three times before degassed toluene 10 mL was added. Then the first generation Grubbs catalyst (10% weight) was added to the solution and the reaction vessel was allowed to put in autoclave at 40°C, H<sub>2</sub> 40 bar and for 40 hours. Then the reaction mixture was precipitated into methanol to afford polymer **6**. The resulting polymer was then purified by redissolving in DCM and precipitating three times in methanol and dried under vacuum to give polymer **6** (271 mg) with 75 % yield. For polymer **6**,  $M_n = 103000$  g/mol and  $D = 1.3$ .<sup>1</sup>

### Synthesis of P2



The N-BOC deprotection of the triblock copolymer **6** was performed as follows: to a solution of **6** (115 mg) in DCM (3 mL) TFA (2 mL) was added and the reaction mixture was allowed to stir for 12h at room temperature. Then the solvent was removed under vacuum and the solid obtained was redissolved in DCM and precipitated into methanol (2x) and then dried under vacuum to give **P2** (54 mg) with 47 % yield. For polymer **P2**,  $M_n = 76000$  g/mol and  $D = 1.2$ .<sup>1</sup>

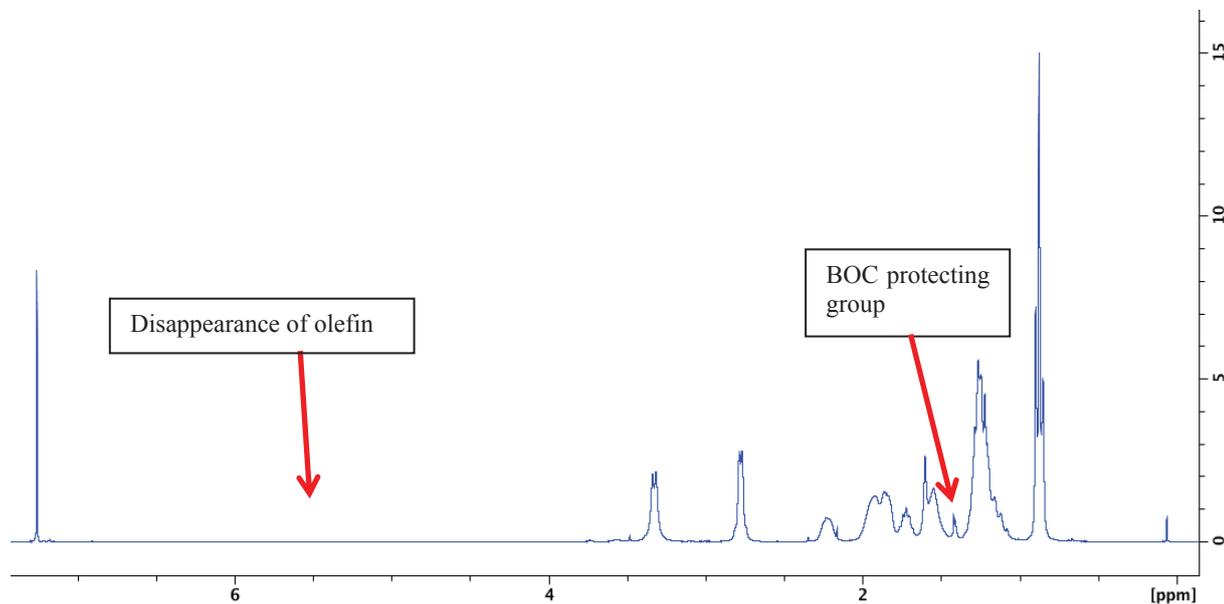


Figure S3:  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ) spectrum of polymer **6**. The disappearance of the double bond after hydrogenation (m, 5.93-5.38 ppm) can be observed in the spectrum.

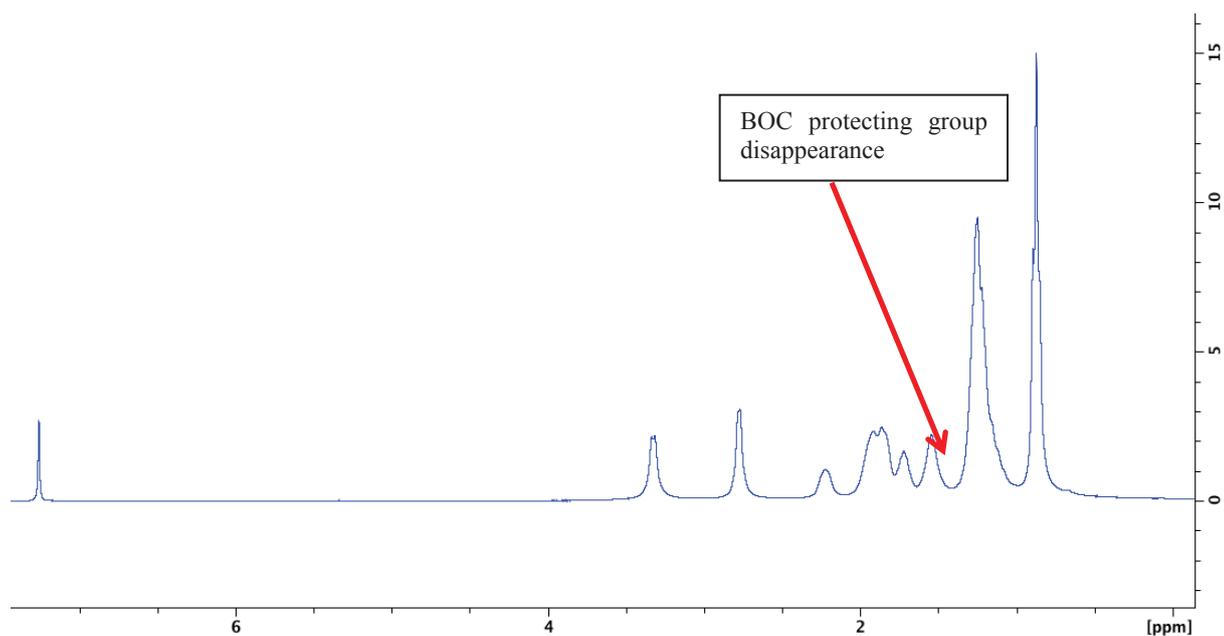


Figure S4:  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ) spectrum of polymer **P2**. The disappearance of the BOC-protecting group after its removal (s, 1.4 ppm) can be observed in the spectrum.

**Table S1: The Kuhn lengths and elasticity constants of all polymers used in this study.**

Polymer	Solution	Kuhn length (nm)	Elasticity constant (nN)
P1	DMSO	$0.53 \pm 0.06$	$20 \pm 3$
P2	DCB	$0.48 \pm 0.04$	$10 \pm 1$
cis-PB	methyl benzoate	$0.33 \pm 0.03$	$25 \pm 4$

PB	methyl benzoate	$0.44 \pm 0.02$	$16 \pm 2$
PE	methyl benzoate	$0.56 \pm 0.04$	$30 \pm 5$
PS	methyl benzoate	$0.81 \pm 0.06$	$47 \pm 5$

**Table S2: Tip/solid substrate chemistries used, isomerization forces and extension increases measured, and percent isomerizations calculated for the mechano-isomerization of P1, PB and *cis*-PB.**

Polymer	Tip/solid	$F_{ct}$ (pN) <sup>a</sup>	$\Delta x_{ct}$ (nm) <sup>b</sup>	L (nm)	$N_{cis,L}$	$N_{ct}$	% isomerization
P1	EF-tip/ EF-silica	Transition (1): 722	(1): 0.4	(1): 98.8	(1): 42	(1): 4	(1): 10
		Transition (2): 850	(2): 2.3	(2): 99.8	(2): 38	(2): 23	(2): 61
P1	EF-tip/ EF-silica	Transition (1): 1005	(1): 2.9	(1): 177.9	(1): 75	(1): 29	(1): 38
		Transition (2): 960	(2): 0.4	(2): 181.2	(2): 46	(2): 4	(2): 9
P1	EF-tip/ EF-silica	951	1.7	76.7	33	17	52
P1	EF-tip/ EF-silica	707	0.9	173.0	73	9	12
P1	EF-tip/ EF-silica	1280	0.6	310.7	132	6	5
P1	EF-tip/ EF-silica	504	0.9	512.3	217	9	4
P1	EF-tip/ EF-silica	640	0.2	53.5	23	2	9
P1	EF-tip/ gold	826	1.5	186.0	79	15	19
P1	EF-tip/ gold	Transition (1): 706	(1): 7.3	(1): 397.9	(1): 169	(1): 73	(1): 43
		Transition (2): 883	(2): 6.4	(2): 409.5	(2): 96	(2): 64	(2): 67
		Transition (3): 1073	(3): 1.8	(3): 420.2	(3): 32	(3): 18	(3): 57
P1	EF-tip/ MF-gold	626	3.8	278.1	118	38	32
P1	EF-tip/ MF-gold	Transition (1): 518	(1): 1.8	(1): 207.9	(1): 88	(1): 18	(1): 20
		Transition (2): 527	(2): 2.3	(2): 209.7	(2): 70	(2): 23	(2): 33
P1	gold-tip/ EF-silica	876	0.6	103.8	44	6	14
P1	gold-tip/ EF-silica	Transition (1): 472	(1): 2.6	(1): 70.0	(1): 30	(1): 22	(1): 20
		Transition (2): 439	(2): 1.1	(2): 72.7	(2): 8	(2): 9	(2): 100
PB	silica-tip/ silica	834	0.4	49.3	49	4	8
<i>cis</i> -PB	silica-tip/ silica	945	1.8	45.8	149	18	12

<i>cis</i> -PB	silica-tip/ silica	Transition (1): 880	(1): 0.4	(1): 62.6	(1): 203	(1): 4	(1): 2
		Transition (2): 1122	(2): 0.6	(2): 63.9	(2): 199	(2): 6	(2): 3
<i>cis</i> -PB	silica-tip/ silica	1180	0.8	162.3	527	8	2

<sup>a</sup>An error of about 80 pN can be estimated for the isomerization force. <sup>b</sup>An error of about 100 pm can be estimated for the extension increase.

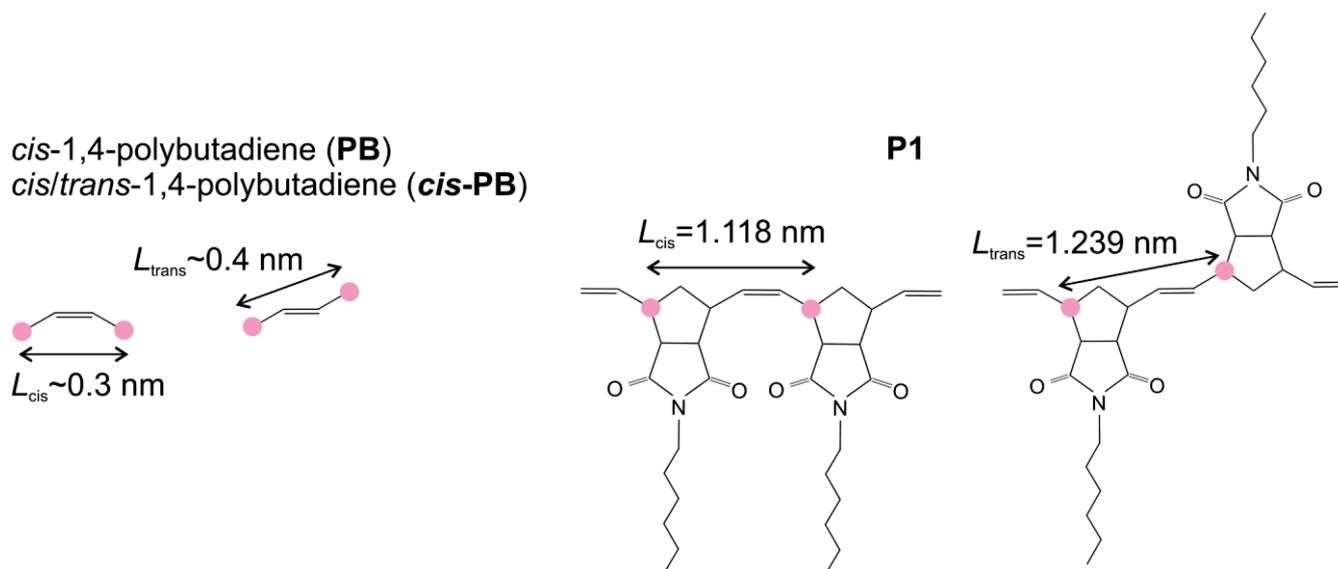
$N_{cis,L}$  is the available number of *cis* double bonds in the contour length. It can be calculated from:

$$N_{cis,L} = \frac{L}{L_{cis} + (1/\alpha - 1)L_{trans}} \quad (1)$$

where  $L$  is contour length of the polymer,  $L_{cis}$  and  $L_{trans}$  are the contour lengths of the *cis* and *trans* isomers respectively (see schematic below), and  $\alpha$  is the percent distribution of the *cis* isomers. **P1**,  $L_{cis} = 1.118$  nm,  $L_{trans} = 1.239$  nm, and  $\alpha = 50\%$ . For **PB** and ***cis*-PB**,  $L_{cis} \sim 0.3$  nm, and  $L_{trans} \sim 0.4$  nm.  $\alpha$  is equal to 36% and 98% in **PB** and ***cis*-PB**, respectively. In cases where more than one isomerization is observed in a single force versus extension profile, the secondary and tertiary  $N_{cis,L}$  is equal to the previous  $N_{cis,L}$  minus the number of isomerized *cis* double bonds,  $N_{ct}$ . The latter can be calculated from:

$$N_{ct} = \frac{\Delta x_{ct}}{L_{trans} - L_{cis}} \quad (2)$$

where  $\Delta x_{ct}$  is the extension increase (Figure 1). Percent isomerization is then  $N_{ct}/N_{cis,L} \times 100$ .



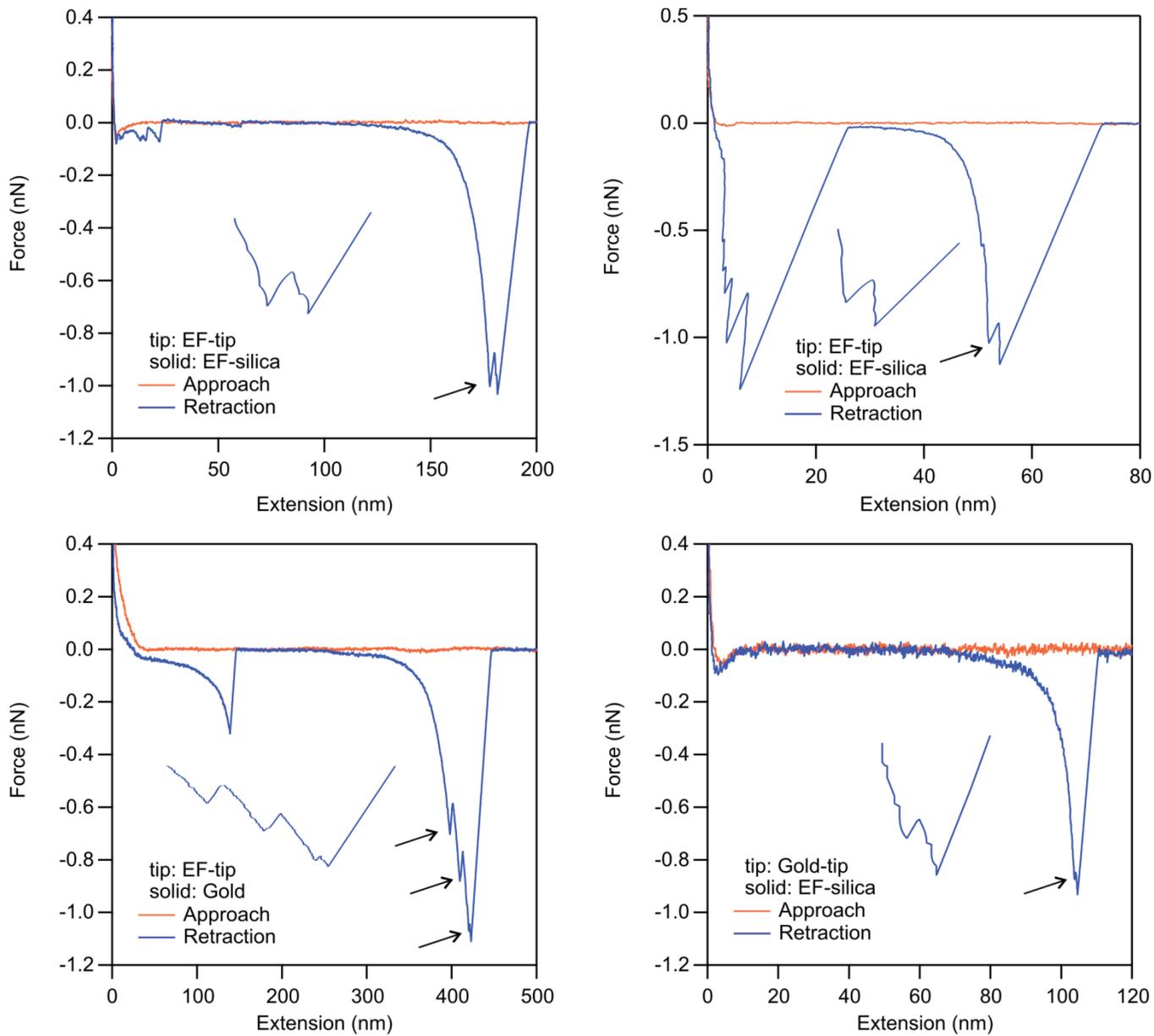


Figure S5: Examples of *cis*-to-*trans* isomerization in **P1** using different AFM tips and solid substrates.

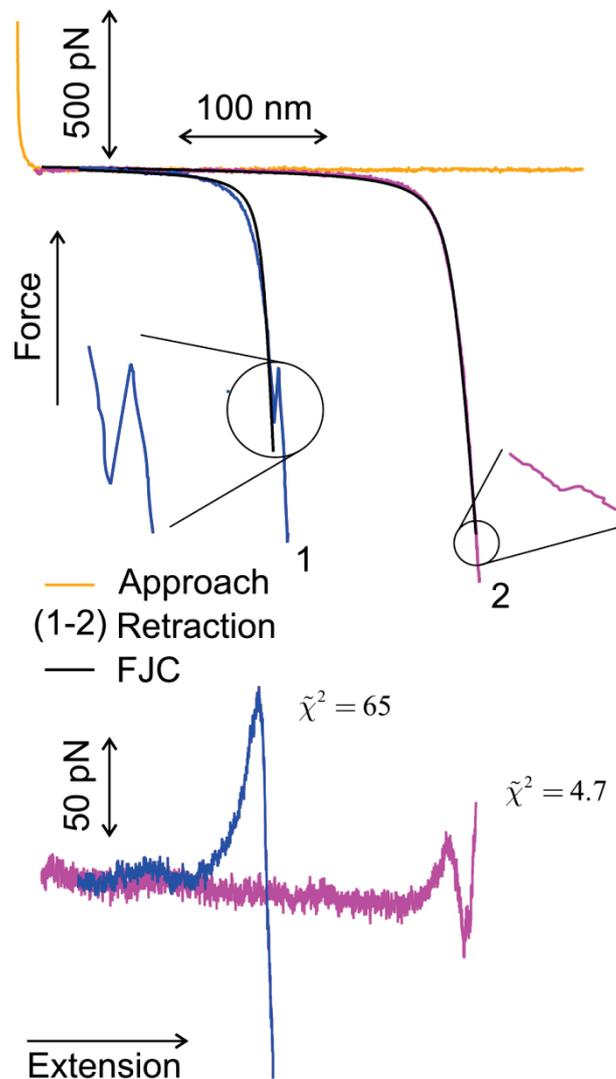


Figure S6: Force versus extension profiles of  $P_1$  with transitions. FJC curve is reproduced using the mean values of the Kuhn length and elasticity constant,  $\ell = 0.53 \text{ nm}$  and  $K = 20 \text{ nN}$ , and is used as comparison agent only for illustration purposes. Orange is a typical approach and 1 and 2 are different retraction curves. The difference between each pre-transition section and the FJC curve is shown below each retraction profile. As a quantitative indicator of the goodness of the comparisons, the reduced  $\tilde{\chi}^2$  statistics is also calculated and added to the differences. Unlike retraction 1 which strongly deviates from the FJC curve; retraction 2 deviates slightly. The difference between retraction 1 and the FJC curve is also obvious by the naked eye from the profiles. Retraction 2 is response from a single molecule.

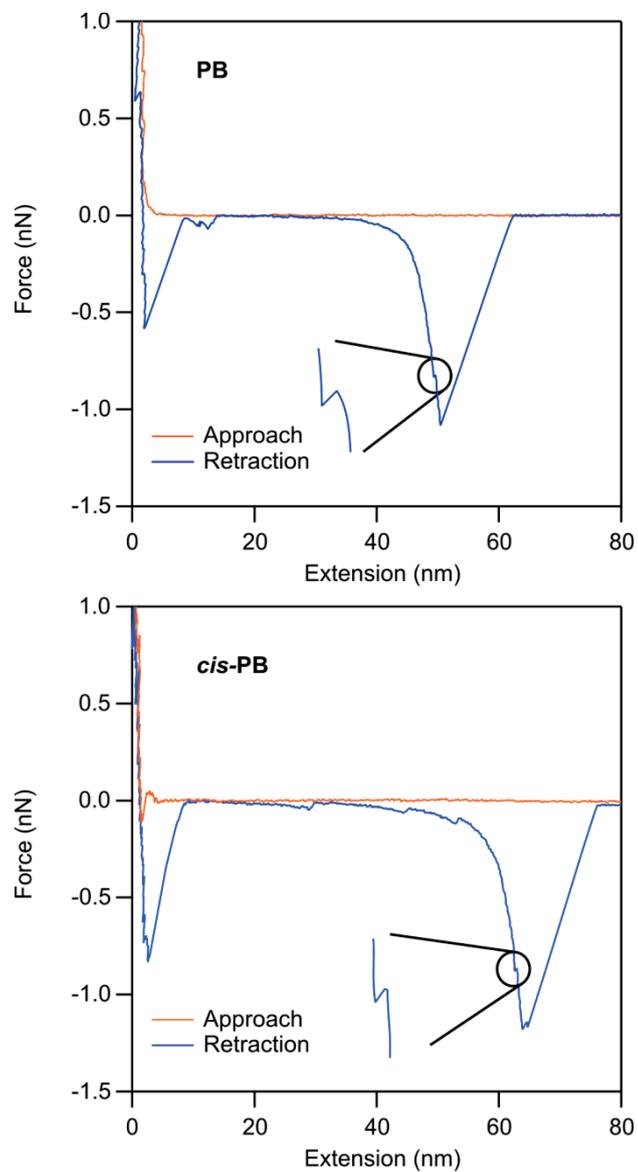


Figure S7: Force versus extension profiles of **PB** and *cis*-**PB** showing isomerization of *cis* double bonds.

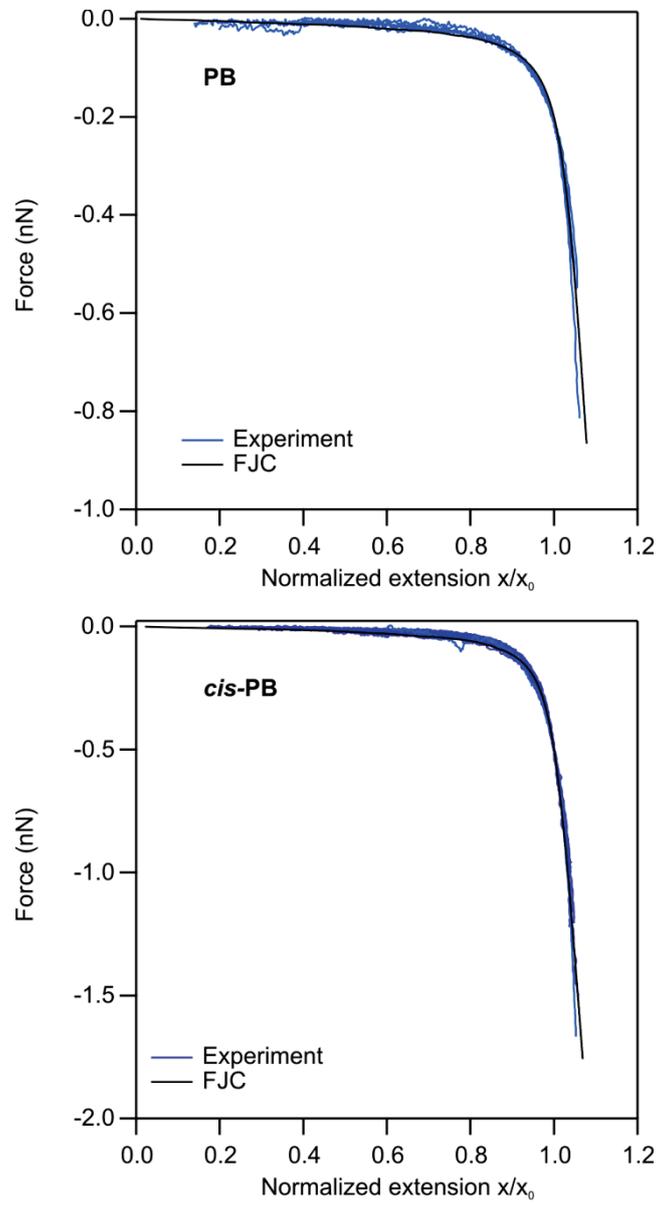


Figure S8: Normalized force versus extension profiles of **PB** and *cis*-**PB** with no isomerization together with the FJC fit. Normalization of the profiles of **PB** is at 200 pN and normalization of the profiles of *cis*-**PB** is at 500 pN.

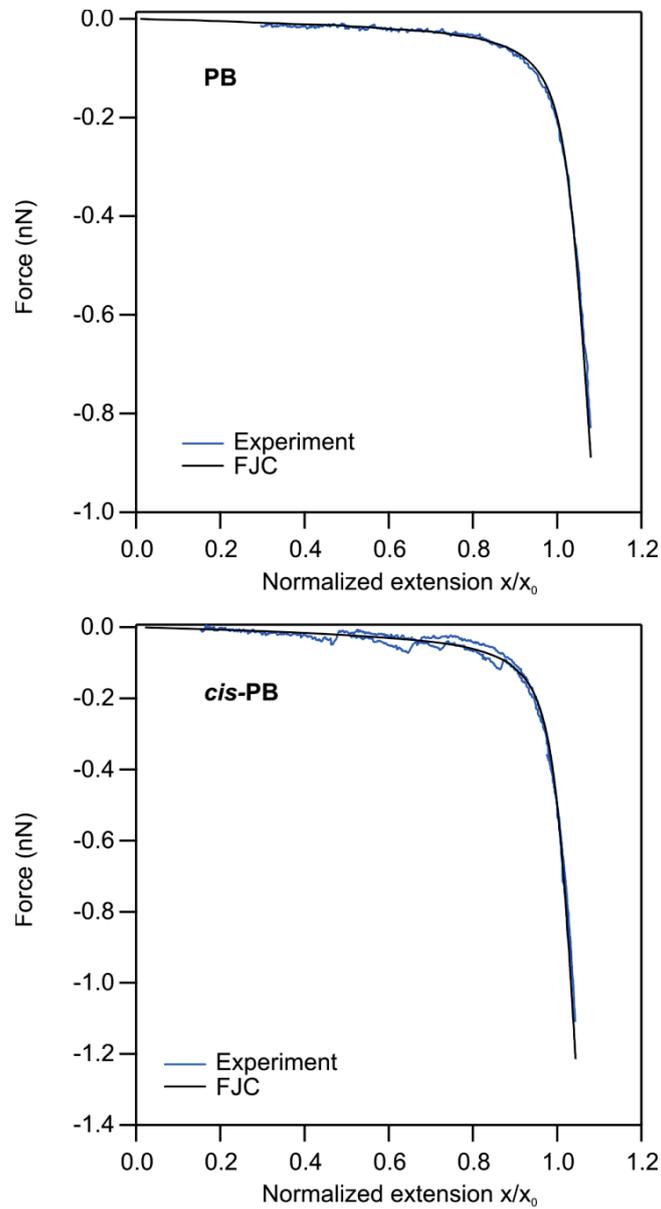


Figure S9: Normalized pre-isomerization sections of different force versus extension profiles of **PB** and **cis-PB** together with the FJC curve. The FJC curve is reproduced using the mean values of the Kuhn length and segment elasticity of each polymer (Table S1).

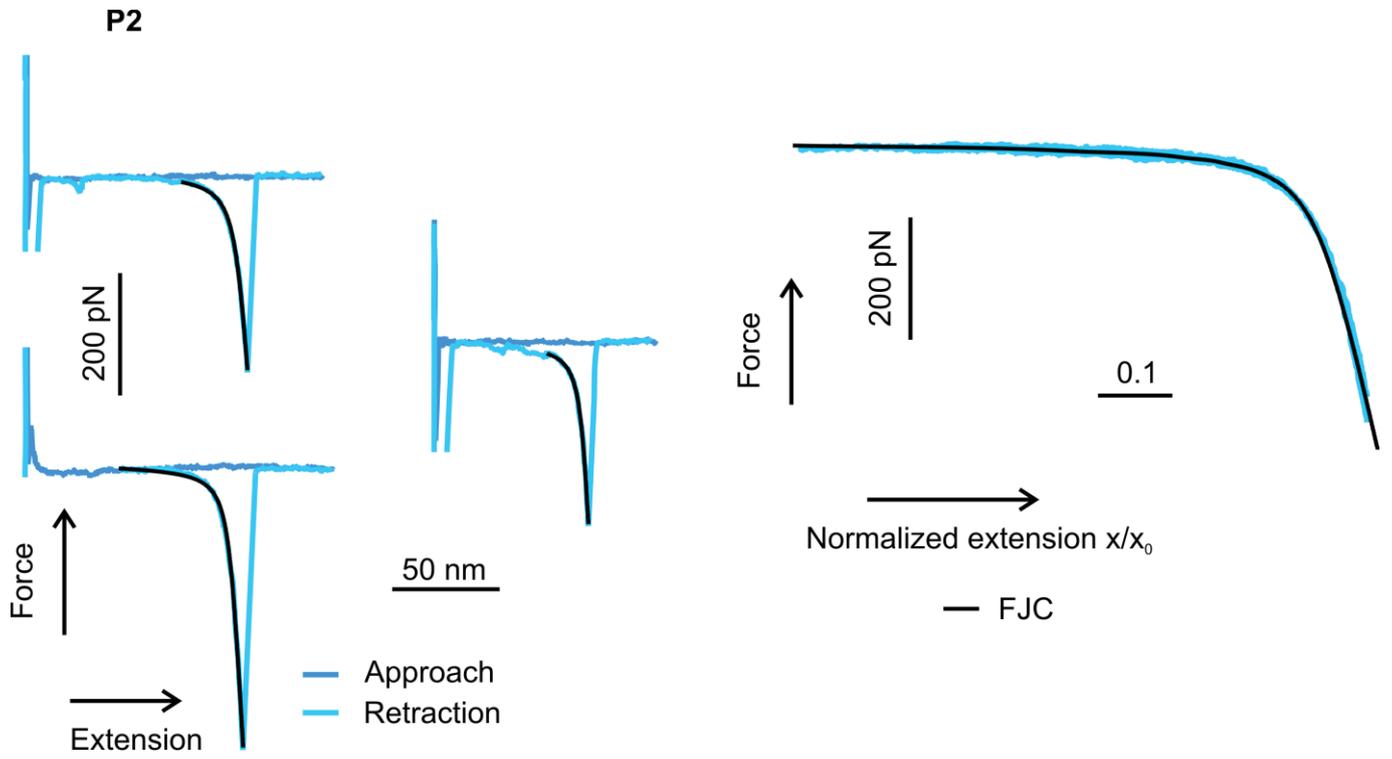


Figure S10: Force versus extension profiles and normalized force versus extension profiles of **P1** together with the FJC curve. The FJC curve is reproduced using the mean values of the Kuhn length and segment elasticity of the polymer (Table S1).

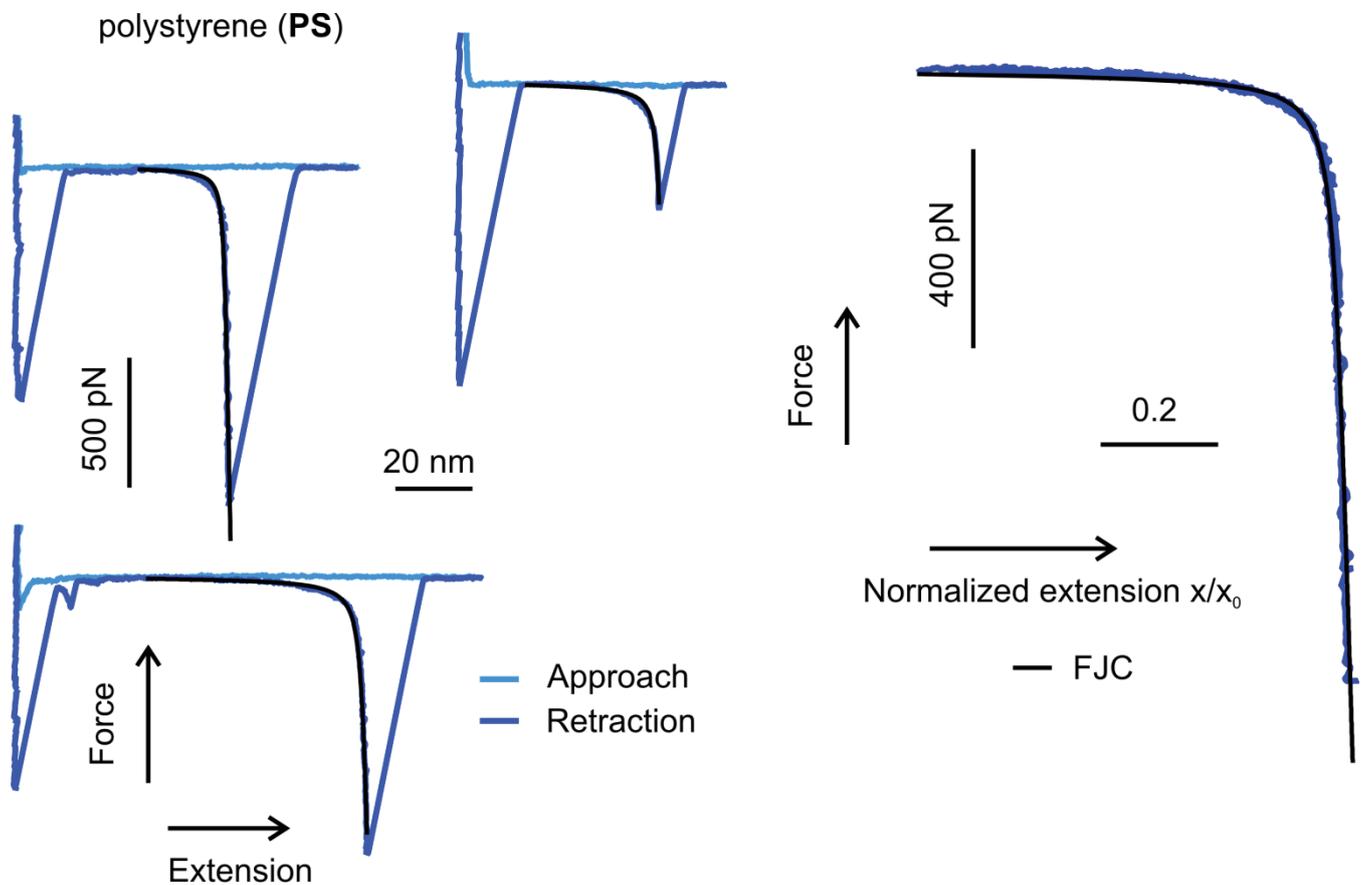


Figure S11: Force versus extension profiles and normalized force versus extension profiles of **PS** together with the FJC curve. The FJC curve is reproduced using the mean values of the Kuhn length and segment elasticity of the polymer (Table S1).

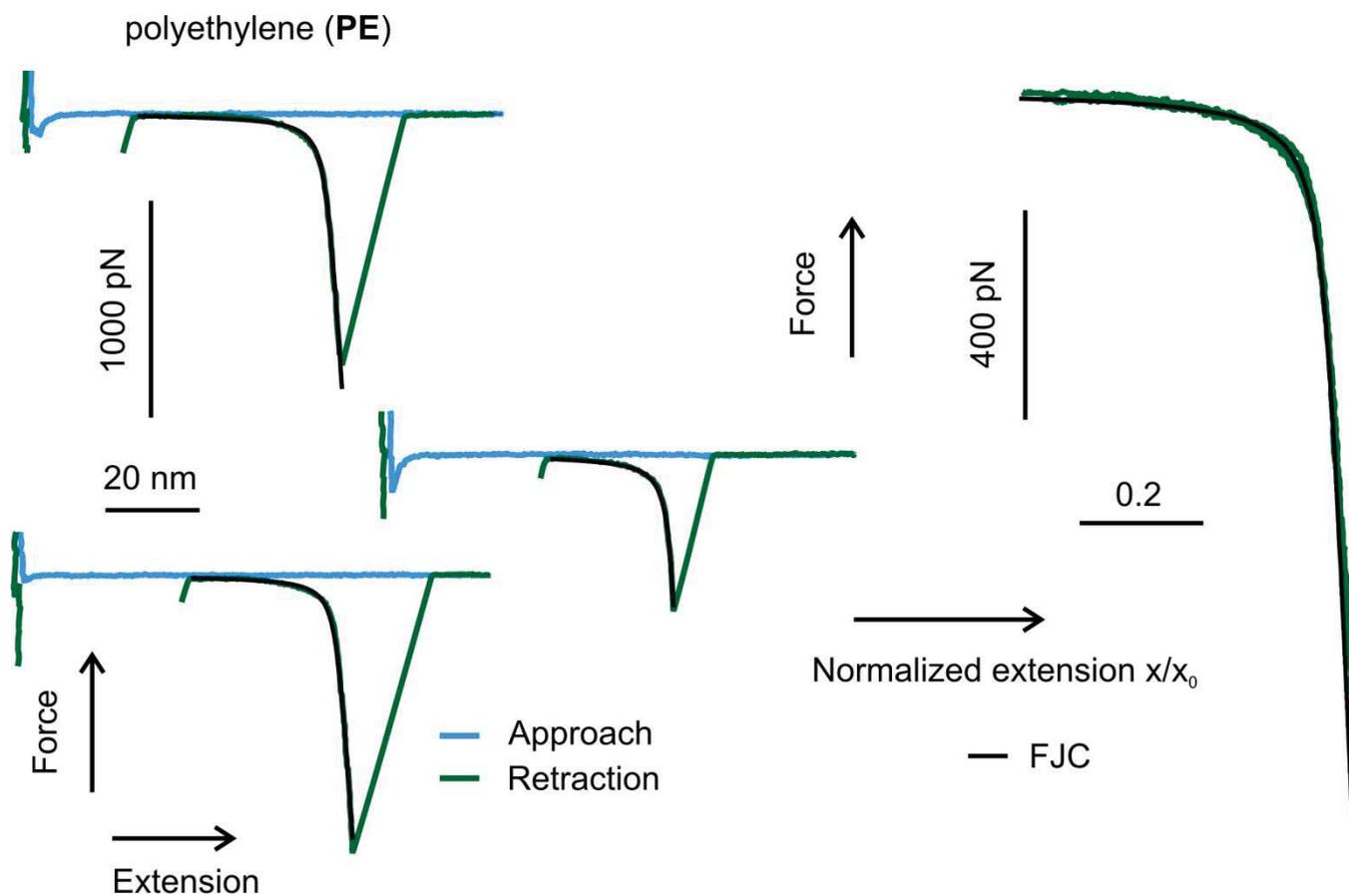


Figure S12: Force versus extension profiles and normalized force versus extension profiles of **PE** together with the FJC curve. The FJC curve is reproduced using the mean values of the Kuhn length and segment elasticity of the polymer (Table S1).

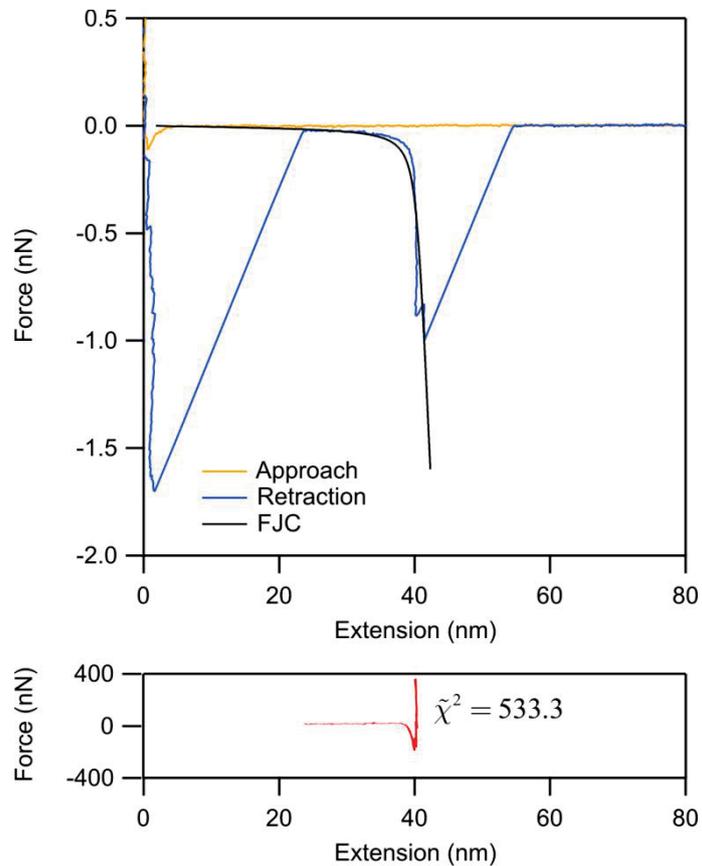


Figure S13: Example of a transition event in the force versus extension profile of **PE** together with FJC curve. The FJC curve is reproduced using the mean values of the Kuhn length and elasticity constant of **PE** ( $\ell = 0.56$  nm and  $K = 30$  nN) and is used as comparison agent only for illustration purposes. The difference between the pre-transition section of the force versus extension profile and the FJC curve is shown below. As a quantitative indicator of the goodness of the comparison, the reduced  $\tilde{\chi}^2$  statistics is also calculated and added to the difference. There is disagreement between the pre-transition section of the force versus extension profile of **PE** and the FJC curve. The disagreement shows that the force versus extension profile is not from a single molecule that is firmly anchored between the AFM tip and the solid substrate.

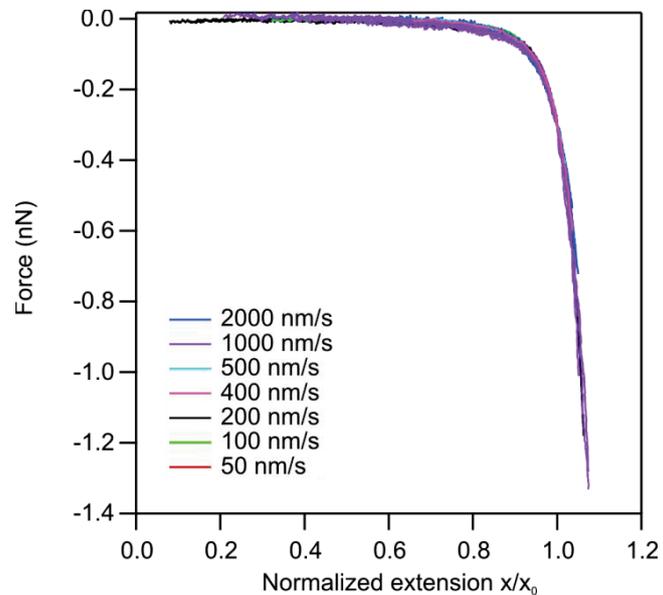


Figure S14: Normalized force versus extension profiles of  $\mathbf{P1}$  at varying pulling velocities.

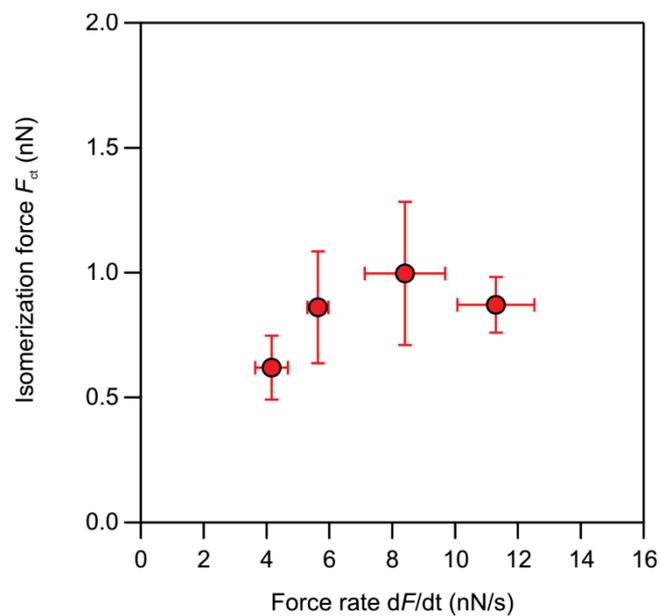


Figure S15: The *cis-to-trans* isomerization force  $F_{ct}$  of  $\mathbf{P1}$  as a function of the force rate  $dF/dt$ .

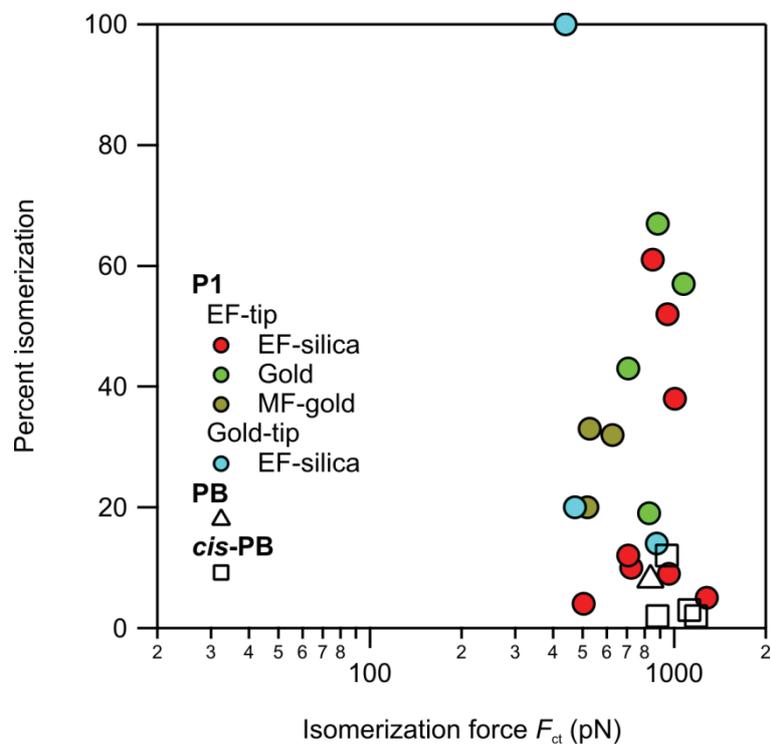


Figure S16: The percent isomerization as calculated in Table S2 as a function of the *cis*-to-*trans* isomerization force  $F_{ct}$ .

## REFERENCES

1. M. Schaefer, N. Hanik and A. F. M. Kilbinger, *Macromolecules*, 2012, **45**, 6807-6818.
2. F. M. Pfeffer, T. Gunnlaugsson, P. Jensen and P. E. Kruger, *Org. Lett.*, 2005, **7**, 5357-5360.
3. D. Muller, I. Zeltser, G. Bitan and C. Gilon, *J. Org. Chem.*, 1997, **62**, 411-416.
4. Y. S. Rim and W. Nudenberg N-(o or p-thiophenyl) substituted polyhalo-5-norbornene-2,3,-dicarboximide flame retardants and polymers containing said imides. 1977, United States Patent Office.