Electronic Supplementary Information

Activated Dopamine Derivatives as Primers for Adhesive-Patch Fixation of Bone Fractures

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Cytotoxicity Study

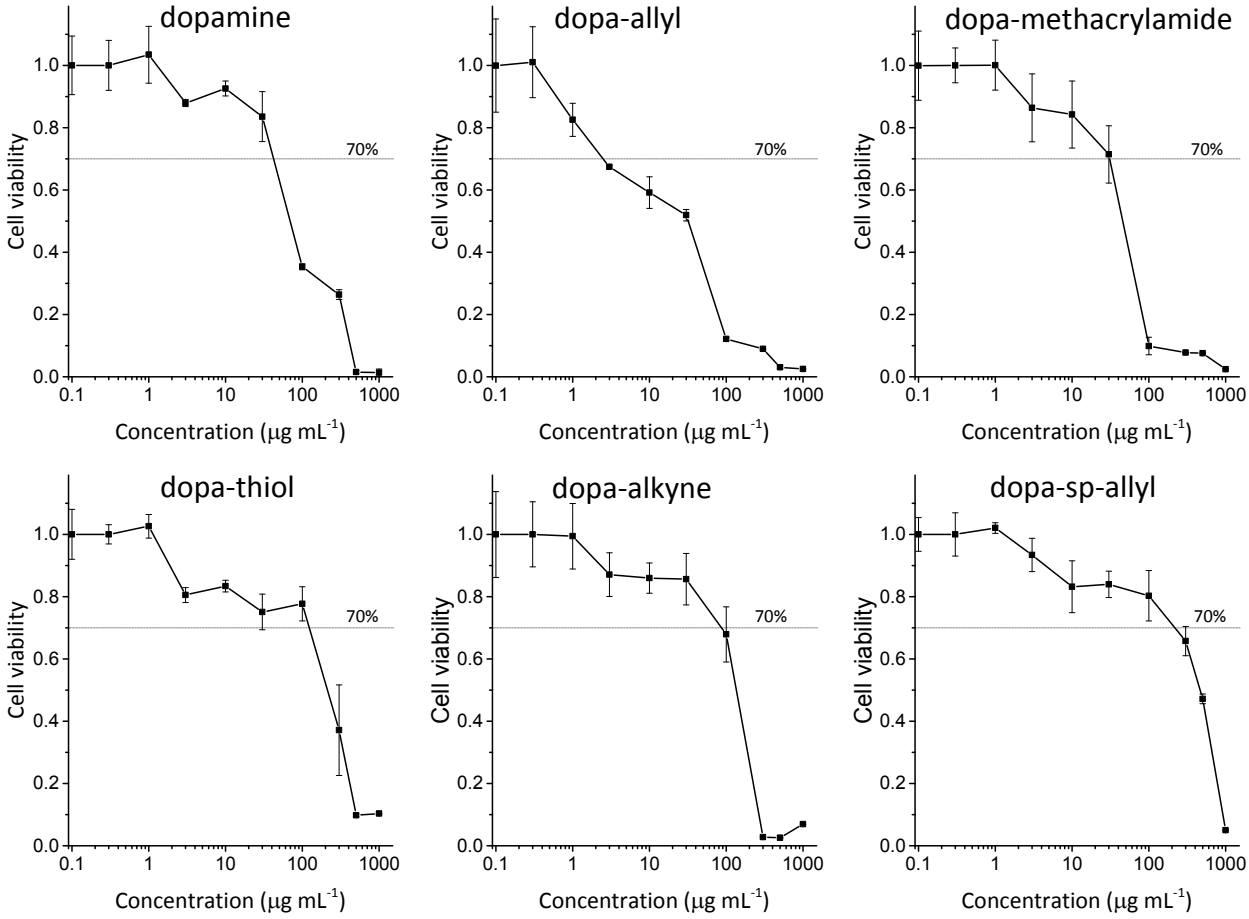

Figure S1. Cell viability of hDFs as a function of concentration (μg mL^{-1}) of dopamine and activated dopamine derivatives: dopa-allyl, dopa-methacrylamide, dopa-thiol, dopa-alkyne, and dopa-sp-allyl.

Determining surface-free energy from contact-angle measurements

The van Oss-Chaudhury-Good (OCG) theory[3] and Equation S1 were used to determine the surface-free energies of the different primer surfaces and the cured TA-matrix, in accordance with the method described by Volpe *et al.*[4]

$$\gamma_l \left(1 + \cos\theta\right) = 2\sqrt{\gamma_l^d \gamma_s^d} + 2\left(\sqrt{\gamma_l^+ \gamma_s^-} + \sqrt{\gamma_l^- \gamma_s^+}\right) \quad \text{(S1)}$$

Where θ [°] is the measured contact angle and γ is the surface free energy, where subscripts l and s are used to designate between the liquid and the solid, respectively, and superscripts +, -, and d are used to separate the acid, base, and dispersive parameters of the surface free energy.
Contact angles (θ) were measured on spin-coated-primer surfaces and cured TA-matrix surfaces for three different liquids (water, diiodomethane, and ethylene glycol) with known surface-free-energy parameters (γ_l^d ,γ_l^+ , and γ_l^-). The parameters used for the liquids are summarized in Table S1. Equation S1 was then solved for each substrate simultaneously for all three liquids to determine the individual parameters for each substrate.

Table S1. Surface-free-energy parameters for water, diiodomethane, and ethylene glycol.[4]

Liquid	γ_l	γ_l^d	γ_l^+	γ_l^-
Water	72.8	21.8	65.0	10.0
Diiodomethane	50.8	50.8	0.00	0.00
Ethylene glycol	48.0	31.4	1.58	42.5

The total surface-free energy, γ_s , was calculated according to Equation S2 and all calculated parameters are summarized in Table S2.

$$\gamma_s = \gamma_s^d + 2\sqrt{\gamma_s^+ \gamma_s^-} \quad \text{(S2)}$$

Table S2. Calculated surface-free-energy parameters for spin-coated-primer surfaces and cured TA-matrix.

Parameter	TA-matrix	dopamine	Dopa-sp-allyl	Dopa-acetylene	Dopa-allyl	Dopa-methacrylamide	Dopa-thiol
γ_s^d	44.71	37.55	38.09	41.30	39.89	40.85	41.08
γ_s^-	0.95	25.56	24.08	21.13	23.01	10.82	22.41
γ_s^+	0.00	1.07	0.47	0.71	0.84	0.05	0.74
γ_s	44.83	48.00	44.82	49.06	48.67	42.33	49.21

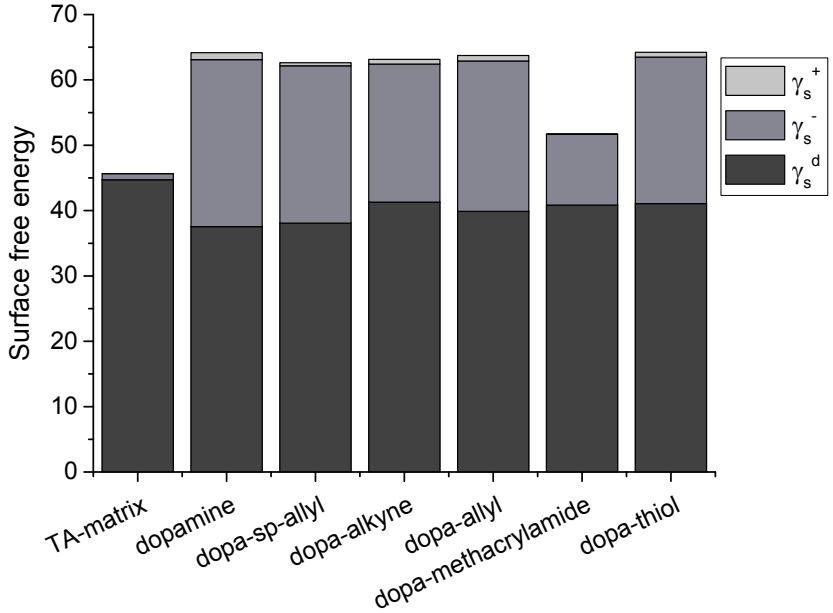

Figure S2. The combined surface energy of glass surfaces spin coated with primer solution, as well as the surface energy of a flat surface of cured TA matrix.

The calculated surface free energies displayed in Figure S3 show that there are some notable differences in the total surface free energy of the different primers. Looking at the individual parts of the surface free energy, especially the acid-base components, γ_s^+, and γ_s^-, it can be seen that dopa-methacrylamide is much more similar to the matrix than the other primer systems are.

Table S3. T-test of results from lap-shear tests of FRAPs calculated in Microsoft Excel using the T-TEST function (type 2). Type 3 of the T-test was used when the similarities in the variances where below 5% (determined by the F.TEST function in Microsoft Excel).

	No primer	DMA (no NaOH)	DSH (no NaOH)	D-sp-A	Dopamine	DAc	DAA	DMA	DSH	DMA + DSH	DAA + DSH	CLEARFIL ™ SE BOND
No primer		1.61%	1.14%	2.28%	29.69%	20.33%	1.94%	0.15%	0.23%	0.02%	0.23%	0.00%
DMA (no NaOH)	1.61%		24.85%	48.08%	1.92%	2.17%	0.71%	0.16%	0.21%	0.10%	0.73%	0.01%
DSH (no NaOH)	1.14%	24.85%		86.69%	2.50%	1.02%	0.24%	0.03%	0.05%	0.01%	0.13%	0.00%
D-sp-A	2.28%	48.08%	86.69%		3.87%	1.44%	0.28%	0.04%	0.05%	0.01%	0.14%	0.00%
Dopamine	29.69%	1.92%	2.50%	3.87%		5.01%	0.37%	0.02%	0.04%	0.00%	0.04%	0.00%
DAc	20.33%	2.17%	1.02%	1.44%	5.01%		9.85%	2.17%	0.74%	0.04%	0.38%	0.00%
DAA	1.94%	0.71%	0.24%	0.28%	0.37%	9.85%		6.27%	4.42%	0.05%	0.29%	0.01%
DMA	0.15%	0.16%	0.03%	0.04%	0.02%	2.17%	6.27%		62.60%	0.15%	0.91%	0.01%
DSH	0.23%	0.21%	0.05%	0.05%	0.04%	0.74%	4.42%	62.60%		0.33%	1.03%	0.03%
DMA + DSH	0.02%	0.10%	0.01%	0.01%	0.00%	0.04%	0.05%	0.15%	0.33%		92.34%	4.85%
DAA + DSH	0.23%	0.73%	1.33% ǂ	0.14%	1.56% ǂ	0.38%	0.29%	0.91%	1.03%	92.34%		25.48%
CLEARFIL ™ SE BOND	0.00%	0.01%	0.00%	0.00%	0.00%	0.00%	0.01%	0.01%	0.03%	4.85%	25.48%	

*Green = Significant difference, Yellow = Close to the significance limit, Red = Differences are not significant ǂ T-test type 3 used.

Effect of addition of NaOH on primer structure

NMR spectra showing the change in structure of primers upon addition of NaOH can be seen in Figure S5 and S6. Addition of NaOH leads to deprotonation of the hydroxyls of the dopa group of dopa-methacrylate (Figure S5) and additionally leads to degradation of the ester bonds in the structure of dopa-alkyne (Figure S6).

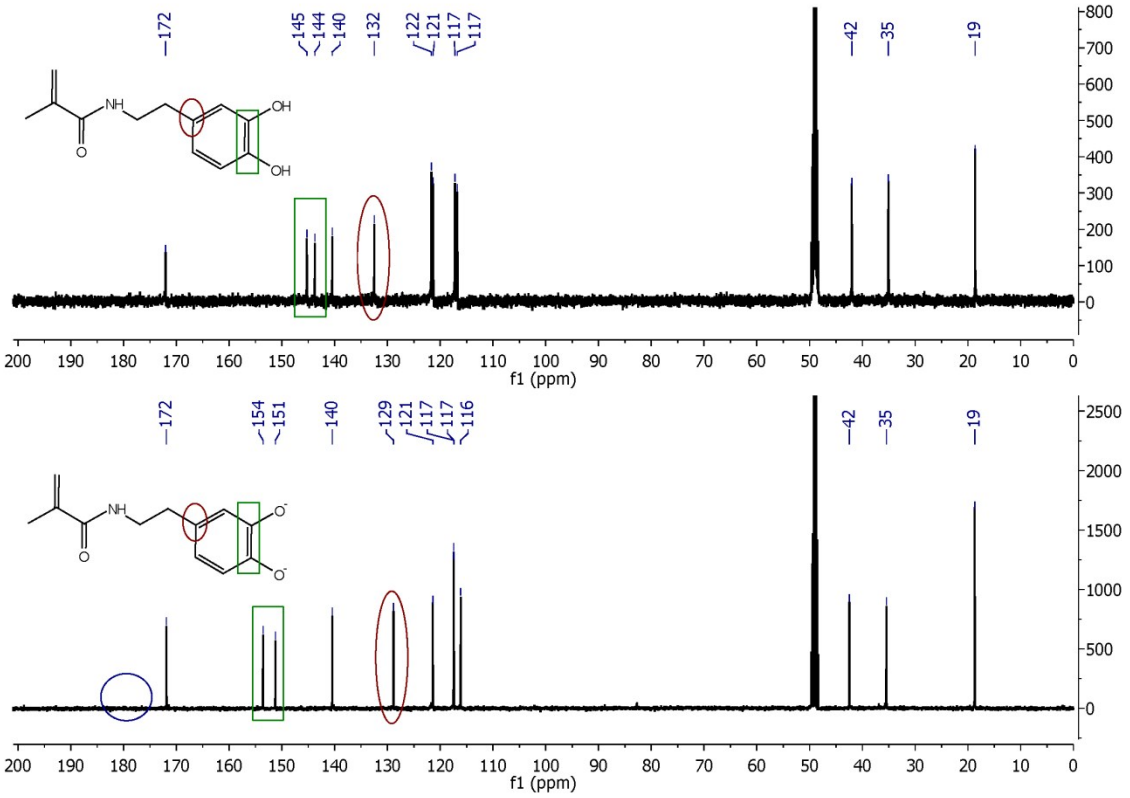

Figure S3. ^{13}C-NMR of dopa-methacrylamide primer in 50:50 D_20/CD_3OD a) before addition of NaOH, and b) after addition of NaOH, showing clear signs of deprotonation of the catechol.

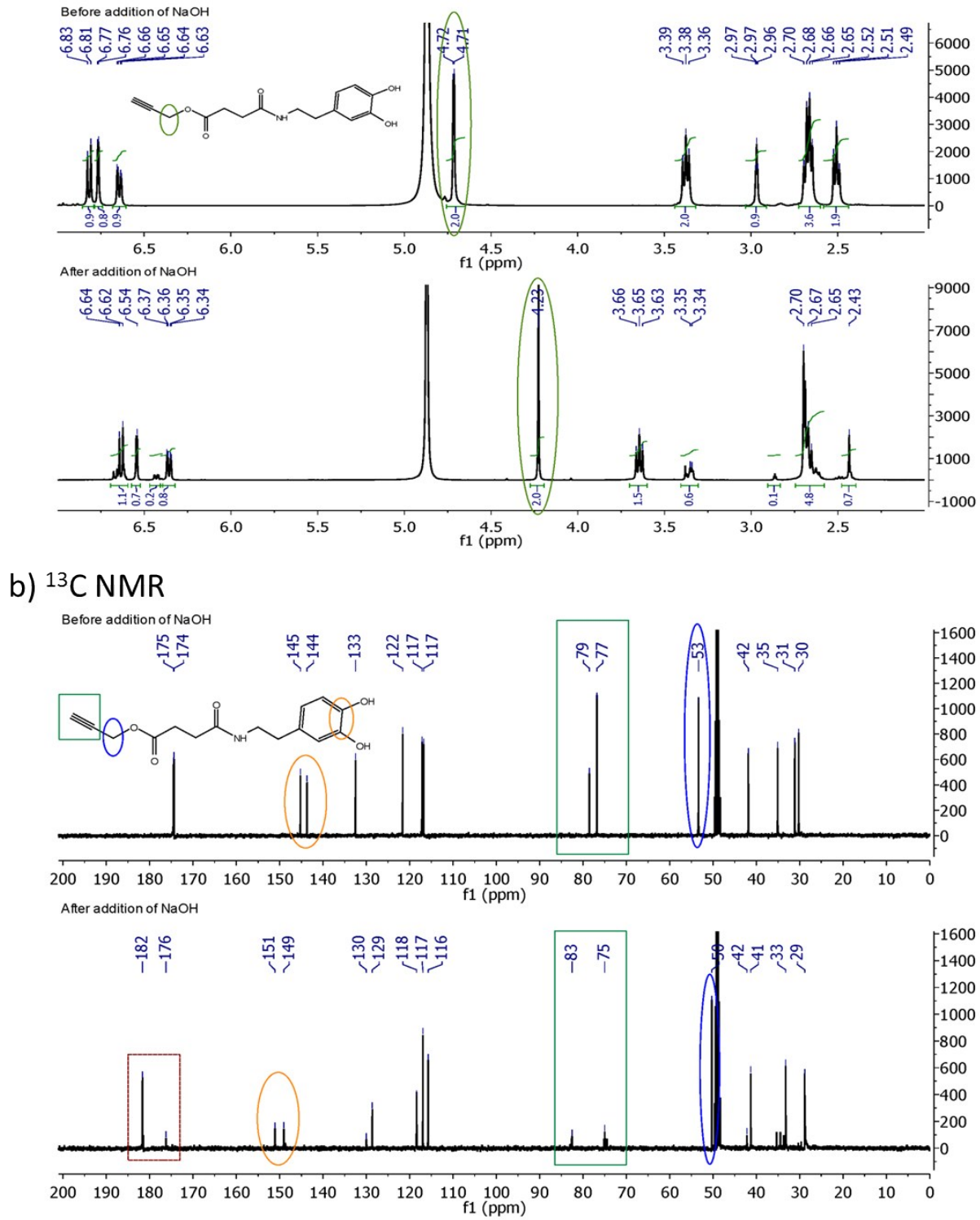

Figure S4. ^{1}H-NMR (a) and ^{13}C-NMR (b) spectra of dopa-alkyne before and after addition of NaOH, showing signs of degradation. (D_2O/CD_3OD used as solvent)

Curing efficiency of TA-matrix

The efficiency of the curing of the TAT-TAA matrix was investigated using RAMAN spectroscopy. As can be seen in Figure S3, RAMAN spectroscopy showed the complete disappearance of peaks corresponding to both allyl and thiol functional groups, indicating full cure of the matrix.

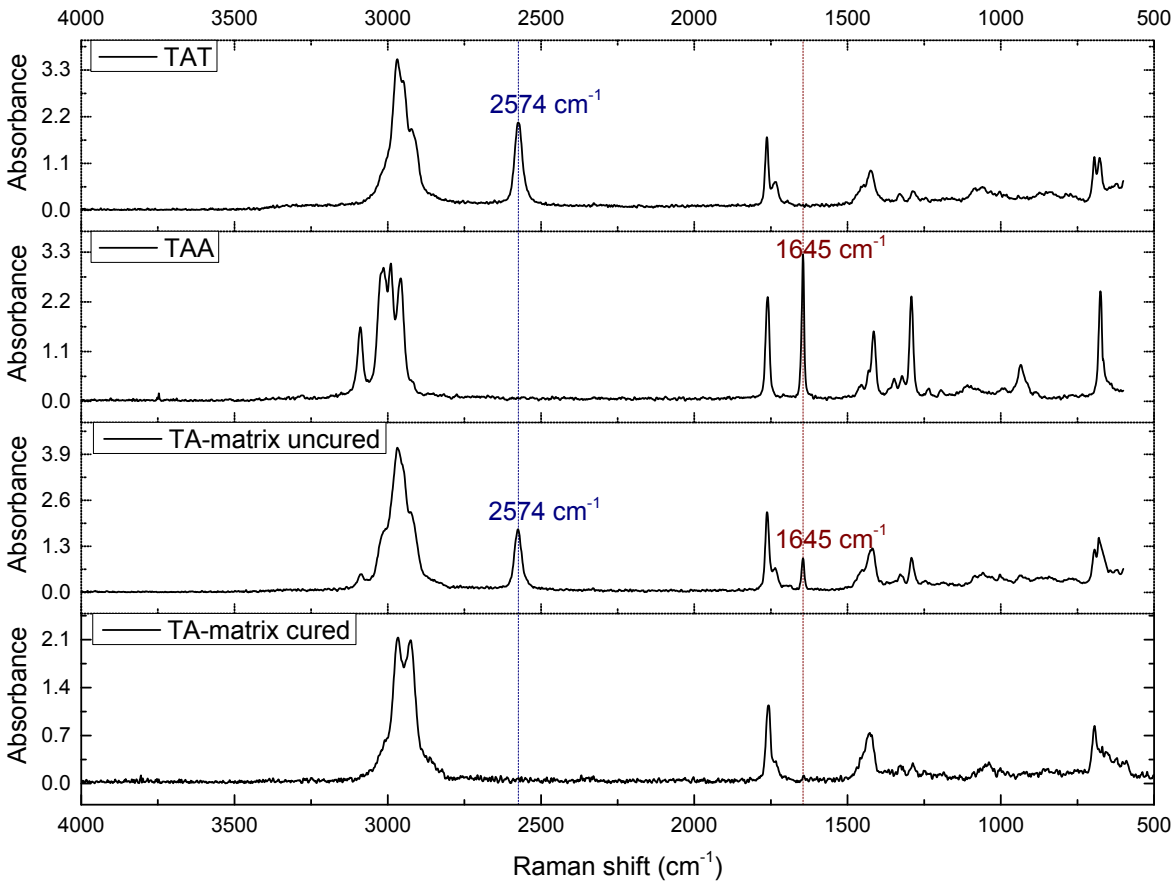

Figure S5. FT-RAMAN spectra of the cured and uncured TA-matrix as well as of the starting materials; TAA and TAT. The Raman shifts corresponding to the thiol and allyl peaks are marked in the figure with dashed vertical lines at 2574 cm^{-1} and 1645 cm^{-1}, respectively.

Adding a layer of dopa-thiol underneath the matrix resulted in reduced curing efficiency of the matrix, as seen in Figure S4., where peaks corresponding to both allyl and thiol are visible even after curing.

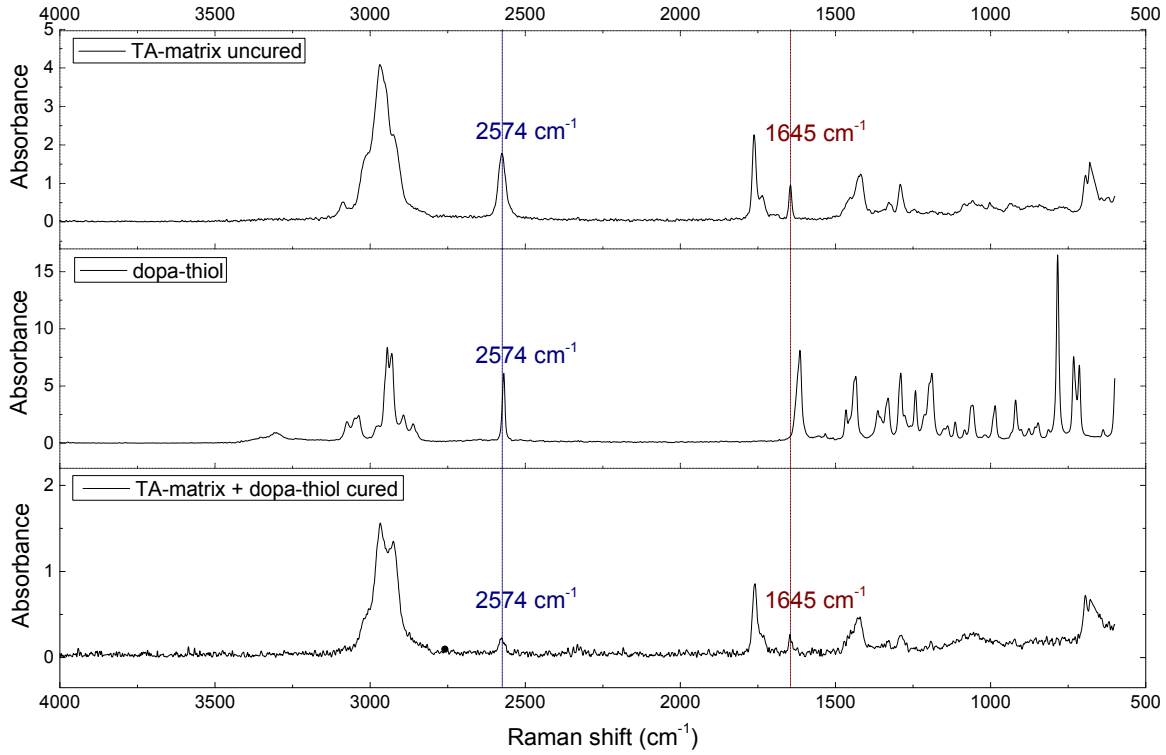

Figure S6. Influence of the addition of a primer layer of dopa-thiol on the curing of the matrix. FT-RAMAN spectra of the TA-matrix, with and without a primer layer of dopa-thiol, were recorded from the primer side of samples cured on glass slides. The low amount of primer compared to TA-matrix made it impossible to see peaks corresponding to the dopa-thiol after curing. However; there were signs that the matrix was not cured to the same extent as when no primer was used.

References (ESI)

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(2) Antoni, P.; Hed, Y.; Nordberg, A.; Nystrom, D.; von Holst, H.; Hult, A.; Malkoch, M. Bifunctional Dendrimers: From Robust Synthesis and Accelerated One-Pot Postfunctionalization Strategy to Potential Applications, *Angew Chem Int Edit*, **2009**, *48*, 2126-2130.

(3) van Oss, C. J. *Interfacial Forces in Aqeous Media*, Marcel Dekker, Inc., New York, USA, **1994**.

(4) Volpe, C. D.; Siboni, S. Some Reflections on Acid–Base Solid Surface Free Energy Theories, *J Colloid Interf Sci*, **1997**, *195*, 121-136.