## Supporting information for

Donor-acceptor covalent organic framework nanofilm-based laser desorption/ionization mass spectrometry for rapid and sensitive determination of creatinine in human serum

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## Materials and reagents

All chemical reagents were of analytical grade. Tetrakis (4-aminophenyl) ethane (ETTA) and 4,4'-(benzo[c] [1,2,5] thiadiazole-4,7-diyl) dibenzaldehyde (TD) were purchased from Jilin Chinese Academy of Sciences-Yanshen Technology Co. Ltd. (Jilin, China). Indium-Tin-Oxide (ITO)-coated glass plate, sinapic acid (SA), gentisic acid (DHB),  $\alpha$ -Cyano-4-hydroxycinnamic acid (CHCA) were purchased from Bruker (Germany). Acetonitrile (ACN) and Ethanol (EtOH) were purchased from Sinopharm Group Co. Ltd. (Shanghai, China). The LC-MS grade acetonitrile (ACN) was purchased from Merck KGaA, Germany. Creatinine (Cre), 9-aminoacridine (9-AA) were purchased from Sigma-Aldrich (USA). Creatinine-D3 (Cre-d3) was purchased from C/D/N Isotopes Inc. (Canada). Acetic acid (HAc), alanine (Ala), serine (Ser), tryptophan (Try), tyrosine (Tyr), aspartic acid (Asp), glutamic acid (Glu), threonine (Thr), valine (Val), dienestrol (NA), estriol (E3), estradiol (E2), hexenoestrol (DES), amlodipine, captopril (CAP), thiopronin, zidovudine (ATZ) were purchased from Aladdin Chemistry Co. Ltd. (Shanghai, China). Bisphenol A (BPA), bisphenol S (BPS), bisphenol F (BPF), bisphenol BP (BPBP), bisphenol B (BPB), bisphenol AF (BPAF), were purchased from Alfa Aesar (UK). The deionised water (resistivity 18.25 M $\Omega$  cm) was prepared by Millipore water treatment system.

## **Characterizations of D-A COF film**

The prepared D-A COF film were charactered using several analytical techniques. X-ray diffraction (XRD) patterns were obtained using a Philips (Netherlands) X'Pert-Pro MPD diffractometer with a scanning range of  $2\theta = 1^{\circ}-30^{\circ}$  at ambient temperature. The morphology and particle size of the prepared films were examined using a MIRA4 field emission scanning electron microscope (SEM, TESCAN, Czech) and a 5500 atomic force microscope (AFM, Hitachi, Japan). Fourier transform infrared (FTIR) spectra were acquired using a Nicolet iS50 spectrophotometer (Thermo Fisher, USA) in the 3800-500 cm<sup>-1</sup> range with a resolution of 4.0 cm<sup>-1</sup>. Ultraviolet-visible (UV-Vis) spectroscopy was employed to measure the optical properties of the prepared films using Cary7000 UV-Vis spectrophotometer (Agilent, USA). A STA449F5 synchrotron thermal analyzer (TGA, Jupiter, Germany) was used to evaluate the thermal stability of the films.



Figure S1. D-A COF nanofilm with different addition of acetic acid reaction volumes:

(A) 5 mL; (B) 2 mL; (C) 0.5 mL; (D) clean ITO glass plate.



Figure S2. (A) Infrared spectra and (B) UV-visible absorption spectra of D-A COF nanofilm.



Figure S3. SALDI-MS spectra of Cre (1.0 mol/L) by using D-A COF nanofilm, CHCA,

9-AA, DHB, and SA as matrices: (A) positive mode; (B) negative mode.



Figure S4. SALDI-MS plots of Cre (1 mmol/L) detected in different NaCl concentrations: (A) 0 mmol/L ; (B) 10 mmol/L ; (C) 50 mmol/L ; (D) 100 mmol/L ; (E) 500 mmol/L ; and (F) 1,000 mmol/L .



**Figure S5.** Images of the formation of co-crystallization of analyte and substrate: (A) water (1.0  $\mu$ L) and D-A COF powder; (B) creatinine sample (1 mmol/L, 1.0  $\mu$ L) and D-A COF powder; (C) water (1.0  $\mu$ L) D-A COF nanofilm; (D) creatinine sample (1 mmol/L, 1.0  $\mu$ L) and D-A COF nanofilm.



**Figure S6.** Reproducibility study: (A) the D-A COF nanofilm substrate based SALDI-MS analysis of 10 consecutive tests at the same sample point, RSD = 3.40%; (B) the D-A COF nanofilm substrate based SALDI-MS analysis of 10 different sample points, RSD = 5.12%; (C) the D-A COF powder substrate based SALDI-MS analysis of 10 consecutive tests at the same sample point, RSD = 43.87%.



Figure S7. Storage stability examination.



Figure S8. The limit of detection (LOD) of Cre , S/N = 3.

Category	Analytes		
Amino acids	Alanine (Ala, MW = 89.09)		
	Serine (Ser, MW = 105.09)		
	Tryptophan (Try, $MW = 204.23$ )		
	Tyrosine (Tyr, MW = 181.19)		
	Aspartic acid (Asp, MW = 133.10)		
	Glutamic acid (Glu, MW = 147.13)		
	Threonine (Thr, $MW = 119.12$ )		
	Valine (Val, MW = 117.15)		
Bisphenolic compounds	Bisphenol A (BPA, MW = 228.29)		
	Bisphenol S (BPS, $MW = 250.70$ )		
	Bisphenol F (BPF, $MW = 200.24$ )		
	Bisphenol BP (BPBP, MW = 352.43)		
	Bisphenol B (BPB, MW = 242.32)		
	Bisphenol AF (BPAF, MW = 336.23)		
	Dienestrol (NA, MW = 266.33)		
Estrogenic	Estriol (E3, MW = 288.38)		
compounds	Estradiol (E2, MW = 272.38)		
	Hexenoestrol (DES, MW = 272.38)		
Drug compounds	Amlodipine (MW = 408.88)		
	Captopril (CAP, MW = 217.29)		
	Thiopronin (MW = $163.20$ )		
	Zidovudine (ATZ, MW = 267.24)		

**Table S1.** 22 small molecule compounds used to examine the properties of low mass regions.

No.	Clinical Scr test (µmol/L)	This method		
		Measurement Concentration (µmol/L)	RSD (%) (n=3)	Recovery (%)
1	49.01	51.25	1.08	104.57
2	53.19	52.72	1.11	99.12
3	54.07	54.27	0.25	100.37
4	52.11	55.14	1.96	105.81
5	57.37	59.03	1.36	102.89
6	63.25	63.14	3.83	99.83
7	66.16	63.86	1.26	96.52
8	67.82	67.85	2.93	100.04
9	69.71	68.07	0.27	97.65
10	67.07	68.50	2.33	102.13
11	72.21	69.24	1.98	95.89
12	85.07	83.70	3.26	98.39
13	80.93	84.27	2.05	104.13
14	91.35	89.91	0.49	98.42
15	89.78	91.34	3.49	101.74
16	91.02	92.56	1.28	101.69
17	92.02	95.89	2.07	104.21
18	102.86	98.69	2.02	95.95
19	102.19	108.62	1.31	106.29
20	132.22	132.25	3.25	100.02
21	136.08	133.04	2.86	97.77
22	146.97	144.74	1.41	98.48
23	153.12	148.68	2.76	97.10
24	160.35	154.15	0.67	96.13
25	169.13	171.50	1.78	101.40
26	175.00	173.70	0.86	99.26
27	202.37	210.18	2.50	103.86
28	227.35	230.75	0.23	101.50
29	263.78	259.12	2.17	98.23
30	377.76	369.46	0.27	97.80

**Table S2.** Determination of Cre in human serum by two methods: Colorimetric MethodBased on the Jaffe Reaction and D-A COF-based LDI-MS Method