SUPPORTING INFORMATION

The versatility of "Click" reactions: Molecular recognition at interfaces

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General Methods

Synthetic reactions were conducted under a dry argon atmosphere. Dry solvents were purchased from ACROS Organics and used as received. Diethylether (Et_2O), hexane and ethylacetate were purchased from VWR and destilled prior to use by common laboratory methods. Ethanol (EtOH), dichloromethane (DCM), dimethylformamide (DMF), and acetonitrile (ACN) used for surface experiments were purchased from Carl Roth or VWR in HPLC grade and used as received. Silica gel 60M (0.04-0.063 mm, Machery-Nagel) was used for column chromatography. Gold substrates used for XPS and NEXAFS were prepared onto polished single-crystal Si(100) wafers which have been precoated with a 9 nm titanium adhesion layer and 30 nm gold. All gold substrates were purchased from Georg Albert PVD and stored under argon prior to use. All surface experiments were performed in gamma-sterilized tubes (Orange Scientific).

Prior to SAM deposition, gold substrates were cleaned in conc. HCl for 6 min and afterwards vigorously rinsed with deionized water and EtOH. SAMs were prepared by immersing substrates into a 1 mM ethanolic solution of 1,2-bis(11-azidoundecyl)-disulfane for 24 h at r.t. and subsequent rinsing with EtOH. The click reaction was performed by dissolving the particular molecule in EtOH so that a 1 mM solution is achieved. Additionally, CuSO4 (0.95 mg, 0.004 mmol) and sodium ascorbate

(=NaAsc, 1.55 mg, 0.008 mmol) were dissolved in 10 mL deionized water. After combining the H_2O and EtOH solutions, the azide SAMs were immersed into the click reaction solution either for 4 days at r.t. or for 2.5 days at 50°C. Afterwards, the samples were rinsed with EtOH, dried in a stream of argon and stored in a container under argon before characterization. Host/guest experiments were performed by immersing the 'clicked' surface into a 1 mM solution of the corresponding counterpart molecule in dichloromethane for 1 h and subsequently immersing it in dichloromethane for 10 min. The reversibility experiment was carried out by immersing the surface in DMF for 10 min. After each step, the samples were immersed in the corresponding solvent (ethanol/water 1:1, DMF or dichloromethane) for another 10 min, dried vigorously in a stream of argon and stored under argon before characterization.

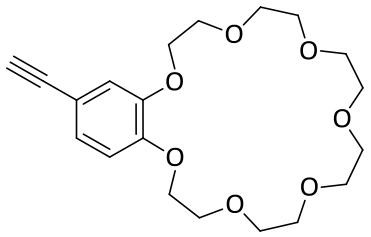
Instrumentation and Data Processing

NMR spectra were acquired on a Bruker ECX 400 (^{1}H at 400 MHz, ^{13}C at 101.8 MHz), a Joel Eclipse 500 (^{1}H: 500 MHz; ^{13}C: 125.8 MHz) and a Bruker 700 (^{1}H: 700 MHz; ^{13}C: 175 MHz) spectrometer at r.t. Exact masses were determined on an ESI-FTICR Ionspec QFT-7, Varian Inc. instrument. Transmission-UV/Vis-spectra were recorded on a Varian Cary 50 UV/Vis spectrophotometer. A spectrum of the underlying SAM was used as background and subtracted from all multilayer spectra.

XPS and NEXAFS measurements have been carried out at the synchrotron radiation source BESSY II (Berlin, Germany). SR XPS (synchrotron radiation XPS) O 1s, N 1s, Au 4f, S 2p, C 1s and F 1s data were acquired by a Scienta 3000 hemispherical electron analyzer (pass energy = 50 eV) at the HE-SGM dipole magnet CRG beamLine. The same beamLine was used for the acquisition of all NEXAFS spectra. An emission angle of 0° was used for all XPS measurements. The binding energy scale of the XP spectra was corrected for static charging using an electron binding energy BE of 83.95 eV for Au $4f_{7/2}$ photoemission of the gold substrate.[1] Peak fitting of XP spectra was performed with a Lorentzian–Gaussian sum function peak shape model using the Unifit 2011 software (Unifit Scientific Software GmbH, Leipzig, Germany). Peak fits and integrated peak areas were obtained after subtraction of a polynomal backgrounds. If not otherwise denoted the FWHM for component peaks in N 1s and C 1s spectra were constrained to be identical. The S 2p core level spectra were fitted with doublets of fixed separation of 1.2 eV, an area ratio of S $2p_{3/2}$:S $2p_{1/2}$ = 2:1 and equal FWHMs for S 2p3/2 and S 2p1/2.[2] NEXAFS spectra were acquired in partial energy electron yield (PEY) mode using a channel plate detector with a retarding field of −150 V [16]. The resolution E/ΔE of the monochromator at the carbonyl π* resonance ((hν = 287.4 eV) was in the order of 2500. Raw spectra were divided by ring current and monochromator transmission, the latter obtained with a freshly sputtered Au sample.[3] Alignment of the energy scale was achieved by using an I_0 feature referenced to a C1s → π* resonance at 285.4 eV measured with a fresh surface of HOPG (highly ordered pyrolytic graphite, Advanced Ceramic Corp., Cleveland, USA). If not otherwise denoted all NEXAFS spectra are shown after subtraction of the pre-edges count rate followed by normalization of the post-edge count rates to one. Both C K- and N K-edges were measured at 30°, 55°, and 90° incident angle of the linearly polarized synchrotron light beam.

Preparation and Characterization of New Compounds

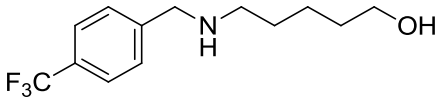
4-Acetylene-substituted benzo[21]crown-7 (CE1)



The Seyferth-Gilbert homologation of **3** under standard conditions yielded **CE1**.[4] 4-Formyl-substituted benzo[21]crown-7 (6.62 g, 17.2 mmol and potassium carbonate (5.24 g, 37.9 mmol) are dissolved in methanol (100 mL) and stirred r.t. After 12 h the solvent is removed under reduced pressure, resolved in ethyl acetate/methanol (2:1) and filtert over celite. The solvent is removed under reduced pressure and afterwards purified using column chromathography (SiO_2, DCM:MeOH, 40:1) yielding 4-acetylene-substituted benzo[21]crown-7 (**CE1**) (5.43 g, 14.3 mmol, yield: 83%).

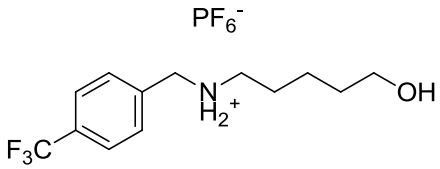
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.94 (s, 1 H), 3.52 – 3.56 (m, 8 H), 3.59 – 3.61 (m, 4 H), 3.64 – 3.68 (m, 4 H), 3.76 – 3.80 (m, 4 H), 4.00 – 4.04 (m, 4 H), 6.67 (d, *J* = 8.3 Hz, 1 H), 6.87 (d, *J* = 1.8 Hz, 1 H), 6.94 (dd, *J* = 8.3 Hz, 1.8 Hz, 1 H) ppm. **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 68.91, 69.02, 69.33, 69.36, 70.28, 70.71, 70.78, 70.88, 70.91, 75.85, 83.45, 113.31, 114.43, 117.24, 125.64, 148.19, 149.56 ppm. **HRMS** (ESI, pos.) m/z: calc. $[M+K]^+$ 419.1456, obs. 419.1467**.**

5-((4-(Trifluoromethyl)benzyl)amino)pentan-1-ol)



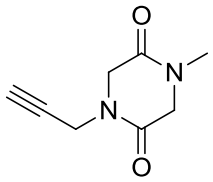
4-Trifluoromethylbenzaldehyde (1.00 g, 5.74 mmol) and 5-aminopentan-1-ol (0.08 g, 7.47 mmol) were refluxed for 24 h in a mixture of 90 mL of abs. ethanol and 60 mL of chloroform. After cooling down to r.t., $NaBH_4$ (2.17 g, 57.40 mmol) was added and the resulting solution stirred at r.t. for another 24 h. The solvent was removed under reduced pressure. The resulting residue was treated with water and the compound was repeatedly extracted with DCM (3 x 50 mL). The organic phase was dried over anhydrous Na_2SO_4 and the solvent was evaporated. Column chromatography (SiO_2, DCM:MeOH, 100:1 to 20:1) afforded 5-((4-(trifluoromethyl)benzyl)amino)pentan-1-ol (1.24 g, 4.75 mmol, yield: 83%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 1.38 – 1.46 (m, 2 H), 1.52 – 1.60 (m, 4 H), 2.01 (s, 2 H), 2.64 (t, *J* = 7.0 Hz, 2 H), 3.62 (t, *J* = 6.5 Hz, 2 H), 3.84 (s, 2 H), 7.44 (d, *J* = 8.0 Hz, 2 H), 7.57 (d, *J* = 8.0 Hz, 2 H)ppm. **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 23.5, 29.6, 32.6, 49.3, 53.5, 62.7, 124.4, 125.5, 128.5, 129.5, 144.2 ppm. **^{19}F NMR** (471 MHz, $CDCl_3$) δ = -62.3 ppm. **HRMS** (ESI, pos. mode) m/z: calc. $[M+H]^+$ 262.1419, obs. 262.1422.

5-Hydroxy-N-(4-(trifluoromethyl)benzyl)pentan-1-aminium hexafluorophosphate(V) (AM2)



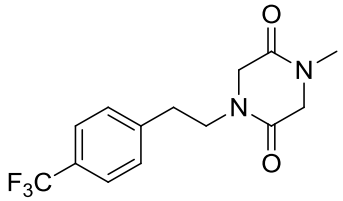
To a solution of 5-((4-(Trifluoromethyl)benzyl)amino)pentan-1-ol (0.31 g, 1.17 mmol) in Methanol (10 mL) conc. HCl was added until a pH < 2 has been reached. Subsequentliy, the solvent has been removed under reduced pressure and the remaining residue was suspended in acetone (30 mL). The addition of saturated aqueous NH_4PF_6 solution yielded a clear solution. After the solvent was removed in vacuo, water (50 mL) has been added. The resulting mixture was stirred at r.t. overnight, filtered, washed with copious amounts of water and dried, yielding 5-Hydroxy-N-(4-(trifluoromethyl)benzyl)pentan-1-aminium hexafluorophosphate(V) (320 mg, 0.78 mmol, yield: 67%) as a white solid. **^{1}H NMR** (400 MHz, CD_3CN): δ = 1.35 – 1.45 (m, 2 H), 1.46 – 1.56 (m, 2 H), 1.64 – 1.74 (m, 2 H), 3.01 – 3.10 (m, 2 H), 3.48 – 3.56 (m, 2 H), 4.23 (t, *J* = 6.3 Hz, 2 H), 7.66 (d, *J* = 8.0 Hz, 2 H), 7.78 (d, *J* = 8.0 Hz, 2 H) ppm.

1-Methyl-4-(prop-2-ynyl)piperazine-2,5-dione (DP1)



Under argon atmosphere, 1-methyl-piperazine-2,5-dione (100.0 mg, 0.78 mmol) was suspended in 60 mL DMF and sodium hydride (37.0 mg, 1.56 mmol) was added stepwise. After stirring for 1 hour at r.t. the reaction mixture was cooled down to 0 °C and tetrabutylammonium iodide (2.0 mg, 0.01 mmol) was added. Afterwards propargyl bromide (100 µL, 1.94 mmol) was added dropwise. After stirring for 12 h at r.t. the reaction was quenched by the addition of a small amount of saturated ammonium chloride solution. The solvent was removed under reduced pressure and the product was purified by using column chromatography (SiO2, DCM/MeOH 97:3) yielding 1-methyl-4-(prop-2-ynyl)piperazine-2,5-dione (130 mg, 0.78 mmol, yield: quant.). **^{1}H-NMR** (400 MHz, DMSO): δ = 2.82 (s, 3H), 3.30 (t, *J* = 2.5 Hz, 1H), 3.96 (s, 2H), 3.99 (s, 2H), 4.17 (d, *J* = 2.5 Hz, 2H) ppm.**^{13}C-NMR** (126 MHz, DMSO): δ = 32.96, 34.25, 49.02, 51.49, 75.68, 78.64, 163.74, 163.91 ppm. **HRMS** (ESI, pos. mode) m/z: calc. $[M+H]^+$ 167.0815, obs. 167.0809, calc. $[M+Na]^+$ 189.0635, obs.189.0633.

1-Methyl-4-(4-(trifluoromethyl)phenethyl)piperazine-2,5-dione (DP2)



Under argon atmosphere, 1-methyl-piperazine-2,5-dione (25.0 mg, 0.20 mmol) was suspended in 15 mL DMF and sodium hydride (15.6 mg, 0.39 mmol) was added stepwise. After stirring for 1 hour at r.t. the reaction mixture was cooled down to 0 °C and tetrabutylammonium iodide (2.0 mg, 0.01 mmol) was added. Afterwards 4-(trifluoromethyl)-phenethyl bromide (82 µL, 0.49 mmol) was added dropwise. After stirring for 12 h at r.t. the reaction was quenched by the addition of a small amount of saturated ammonium chloride solution. The crude product was washed with DCM (3 x 20 mL) and dest. aq. (3 x 20 mL). Organic layers were combined and the solvent was removed under reduced pressure yielding 1-methyl-4-(4-(trifluormethyl)phenethyl)piperazine-2,5-dione (8.0 mg , 0.03 mmol, yield: 14%). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ =, 2.97 – 2.94 (m, 5H) 3.66 – 3.63 (m, 2H), 3.89 (s, 2H), 3.96 (s, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 2H) ppm.**^{13}C-NMR** (126 MHz, $CDCl_3$): δ = 29.8, 33.0, 33.4, 47.4, 50.4, 51.9, 125.7, 125.8, 125.8, 125.9, 129.2, 142.1, 163.2, 163.3 ppm. **HRMS** (ESI, pos. mode) m/z: calc. $[M+Na]^+$ 323.0983, obs. 323.1006.

Original NMR of New Compounds

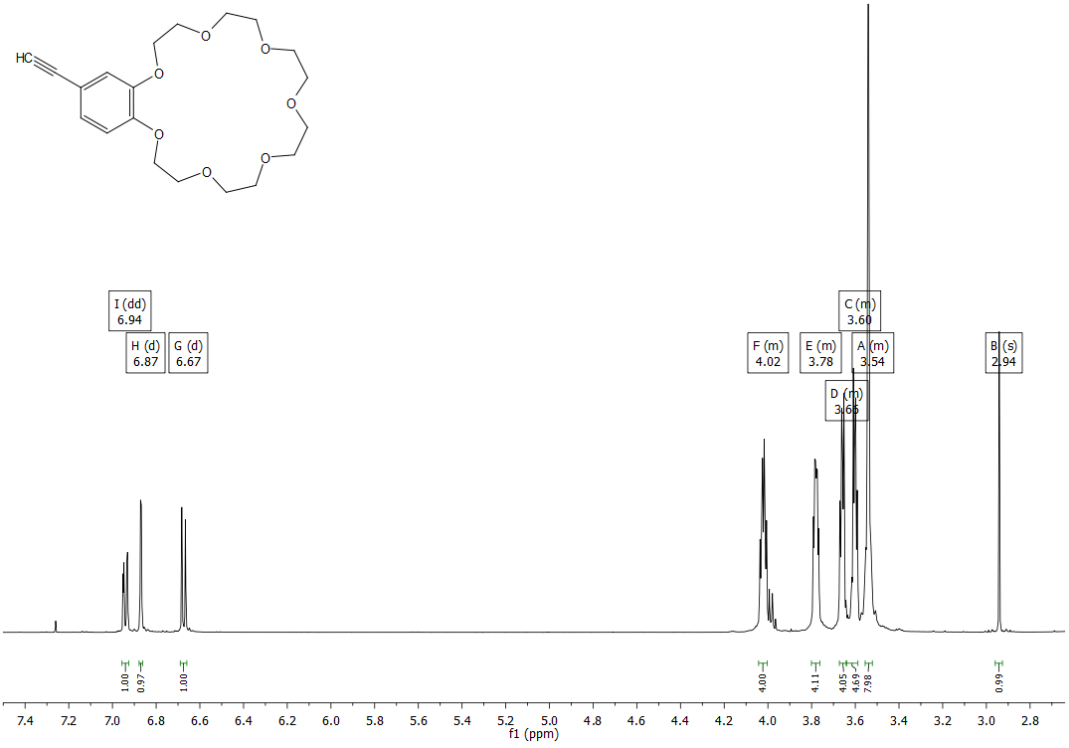


Figure S 1: ^{1}H-NMR spectrum of 4-acetylene-substituted benzo[21]crown-7 (CE1).

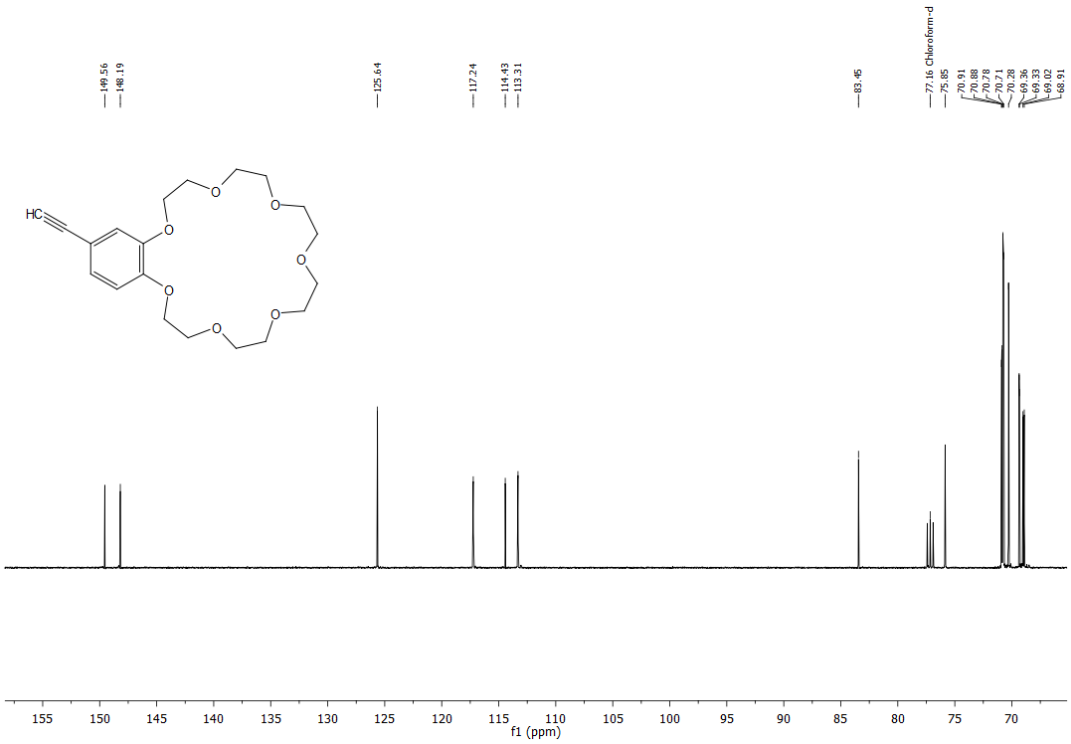


Figure S 2: ^{13}C-NMR spectrum of 4-acetylene-substituted benzo[21]crown-7 (CE1).

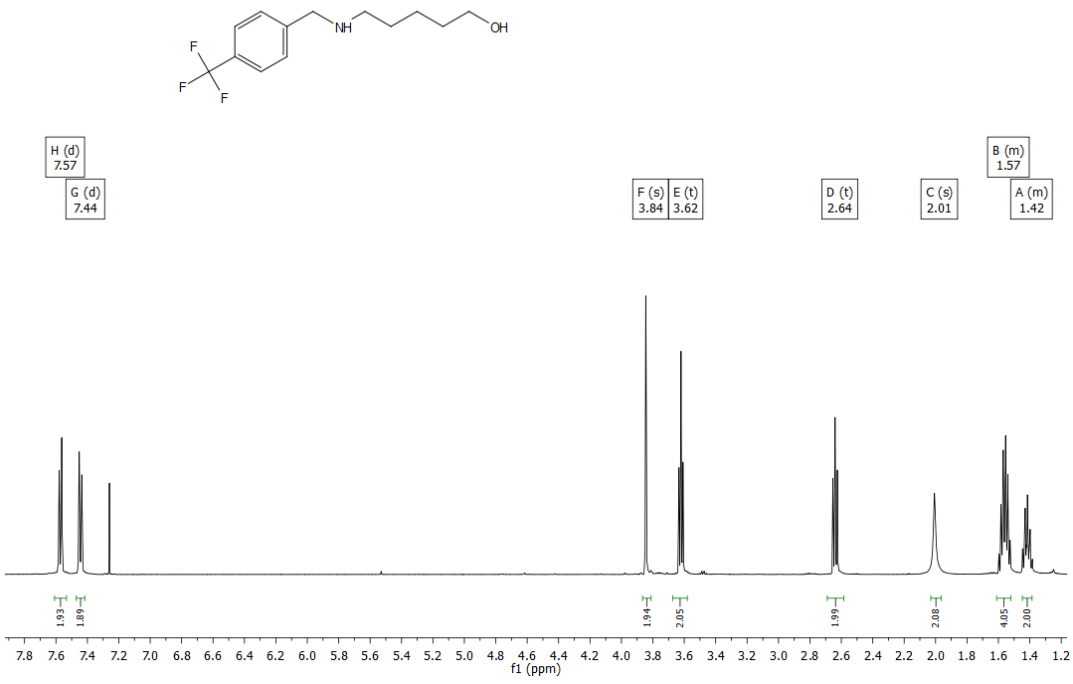


Figure S 3: ^{1}H-NMR spectrum 5-((4-(Trifluoromethyl)benzyl)amino)pentan-1-ol).

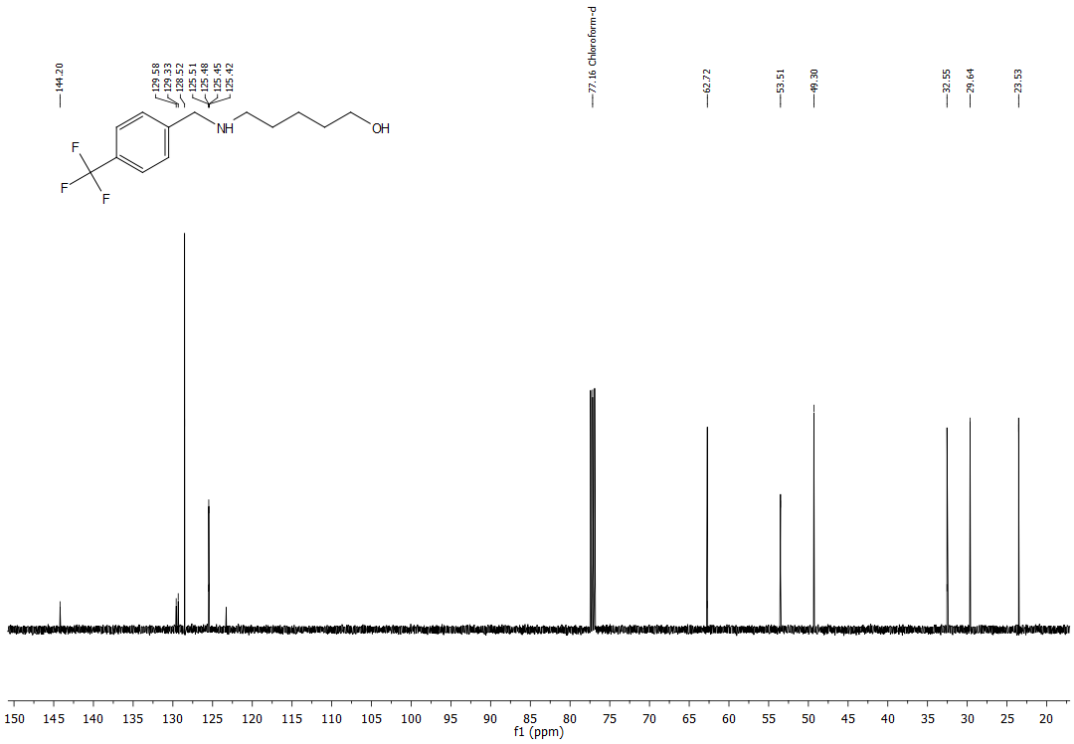


Figure S 4: ^{13}C-NMR spectrum of 5-((4-(Trifluoromethyl)benzyl)amino)pentan-1-ol).

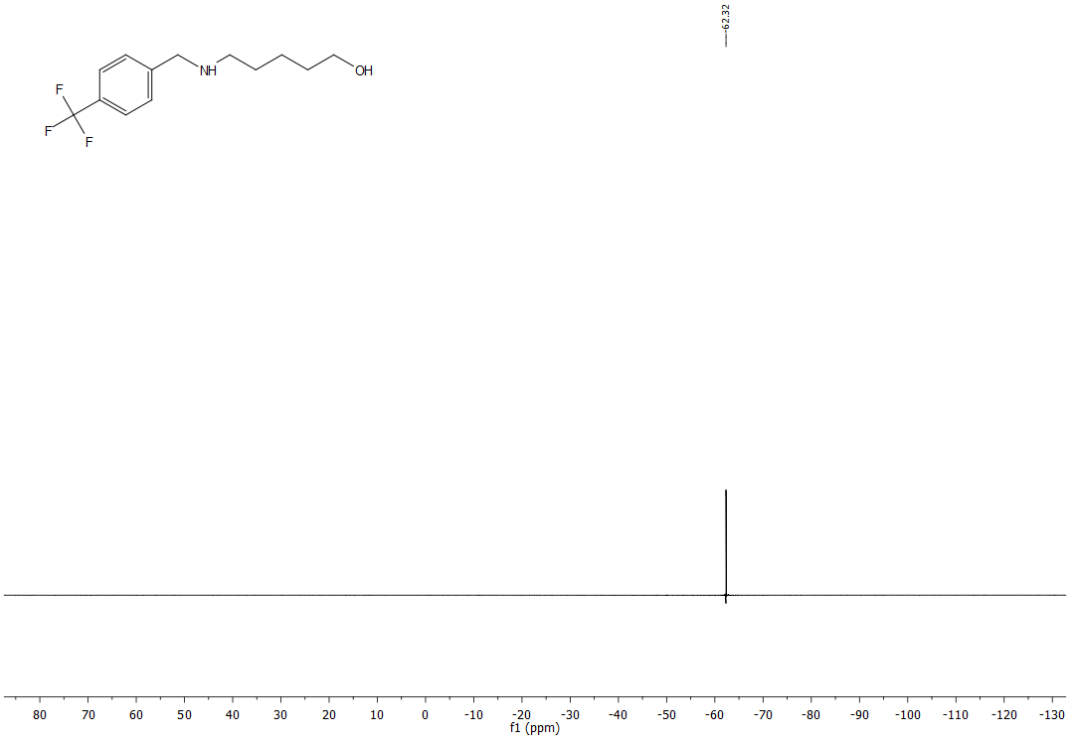


Figure S 5: ^{19}F-NMR spectrum of 5-((4-(Trifluoromethyl)benzyl)amino)pentan-1-ol).

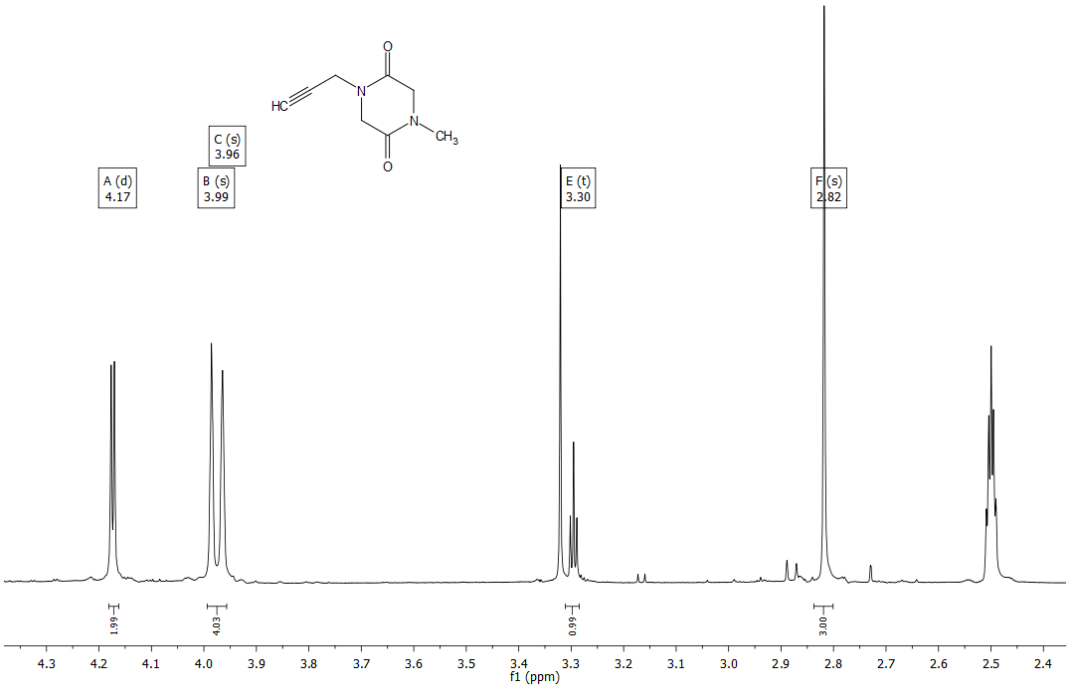


Figure S 6: ^{1}H-NMR spectrum 1-Methyl-4-(prop-2-ynyl)piperazine-2,5-dione (DP1).

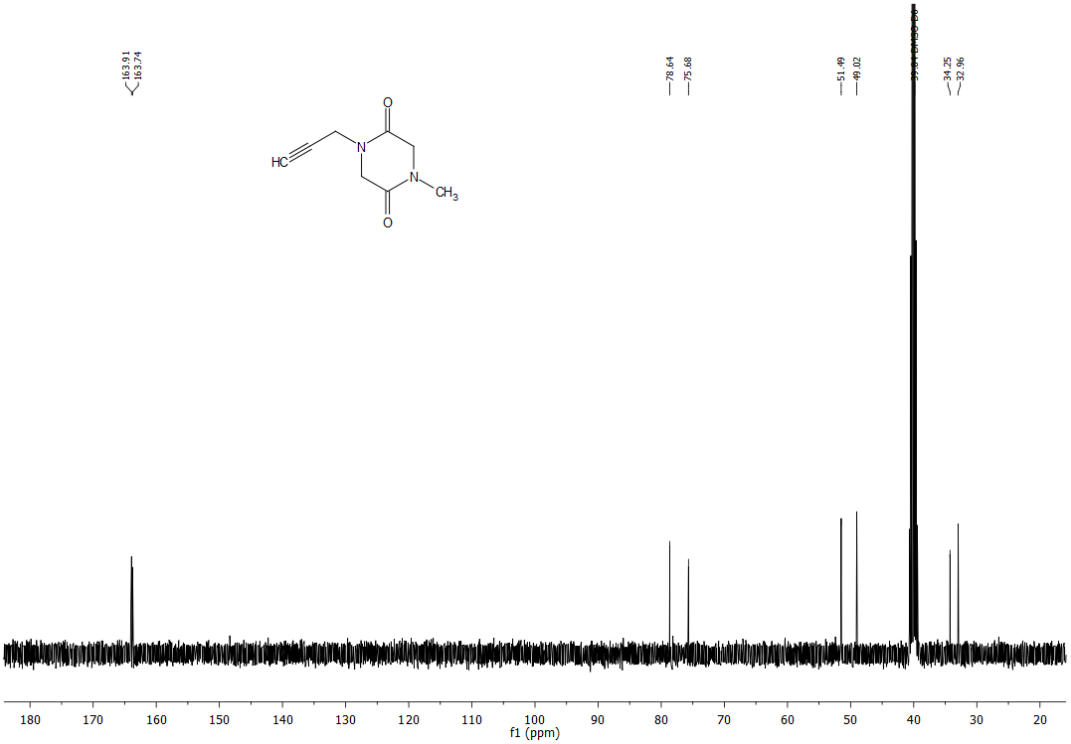


Figure S 7: ^{13}C-NMR spectrum 1-Methyl-4-(prop-2-ynyl)piperazine-2,5-dione (DP1).

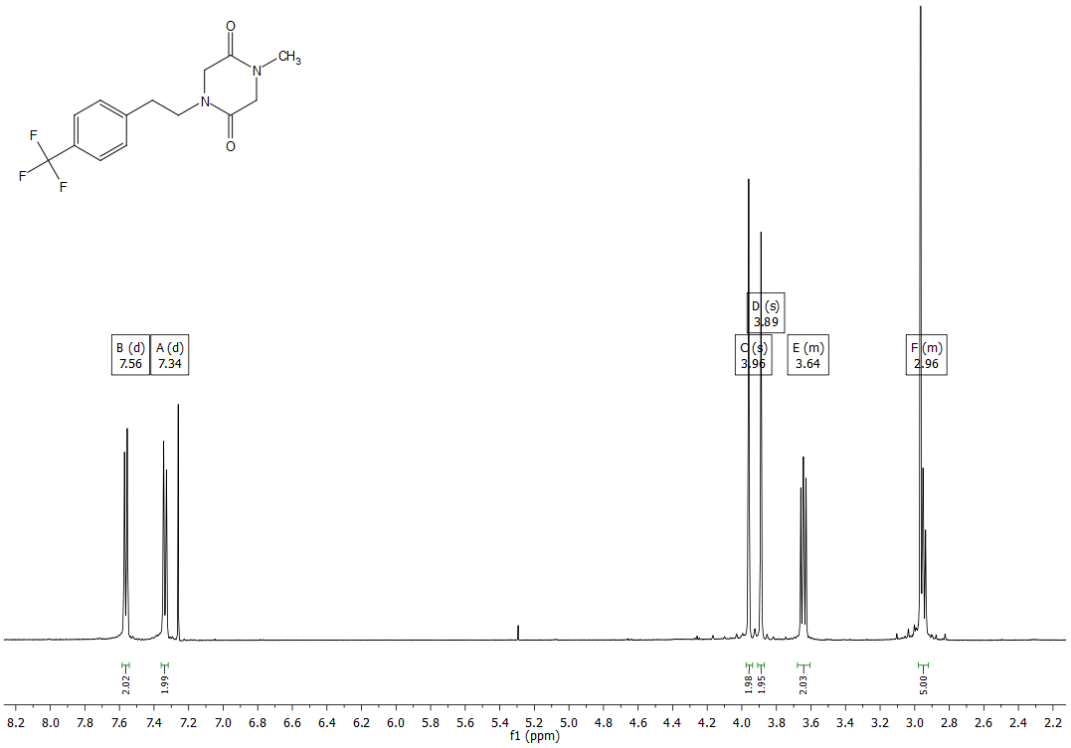


Figure S 8: ^{1}H-NMR spectrum 1-Methyl-4-(4-(trifluoromethyl)phenethyl)piperazine-2,5-dione (DP2).

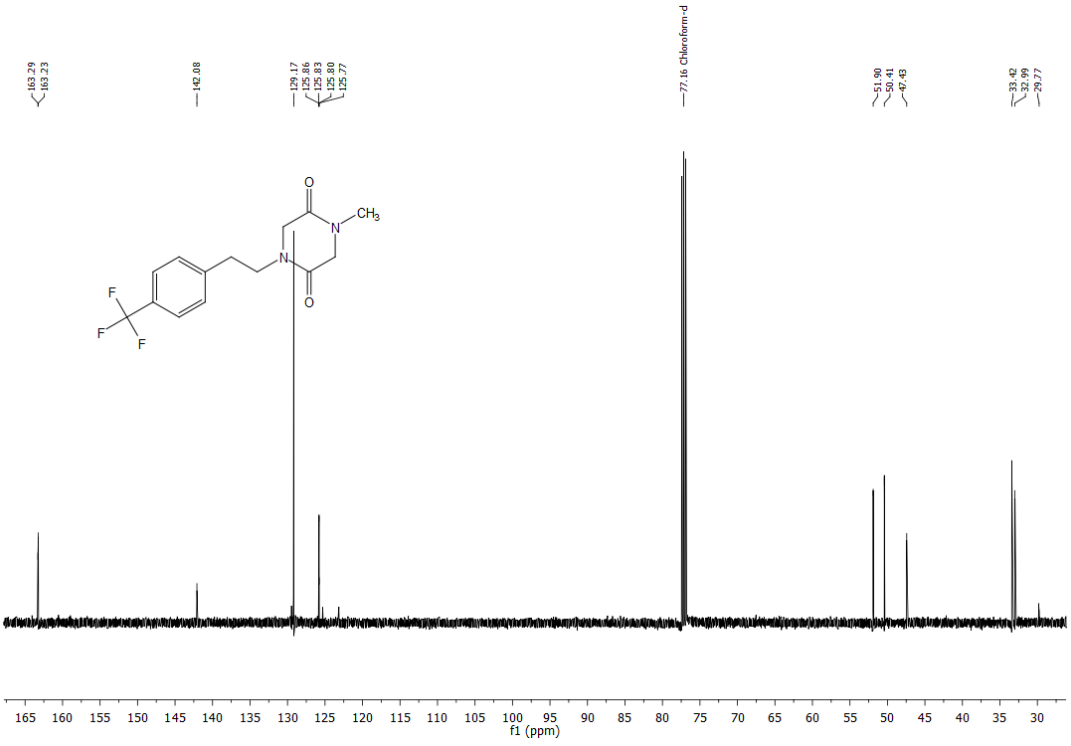


Figure S 9: ^{13}C-NMR spectrum 1-Methyl-4-(4-(trifluoromethyl)phenethyl)piperazine-2,5-dione (DP2).

Additional XPS- and NEXAFS-Data

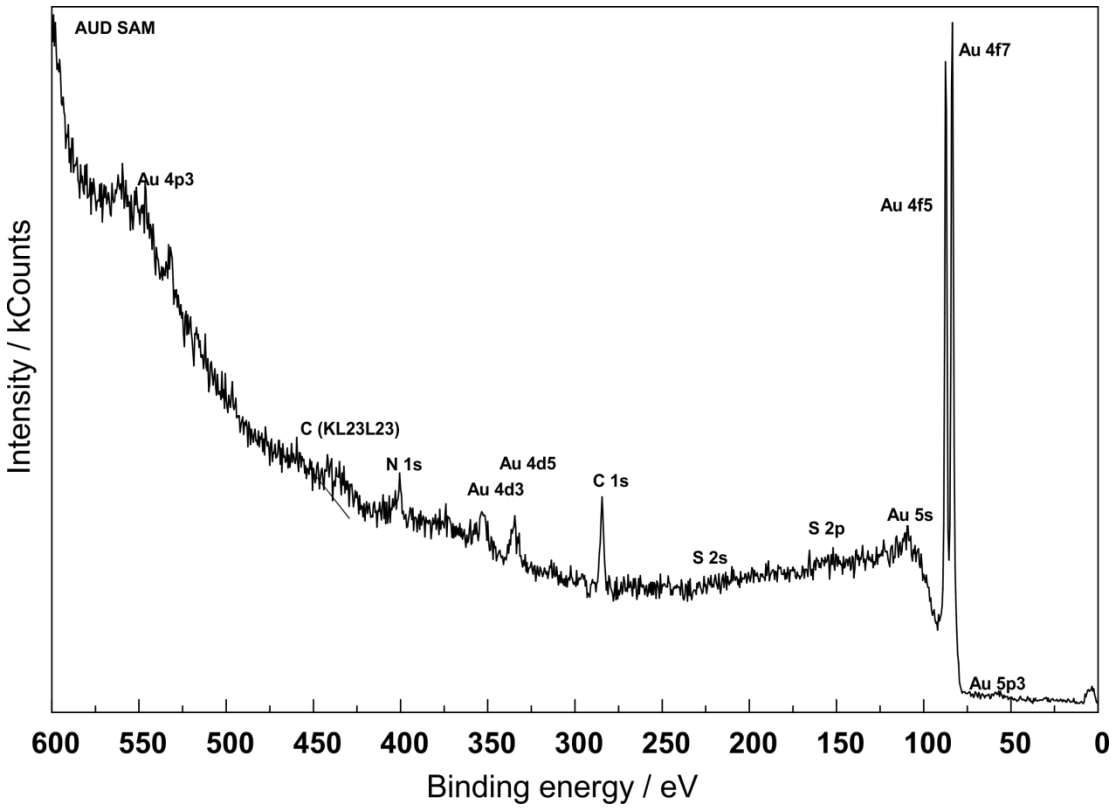


Figure S 10. Survey XP Spectum of AUD (hv = 700 eV).

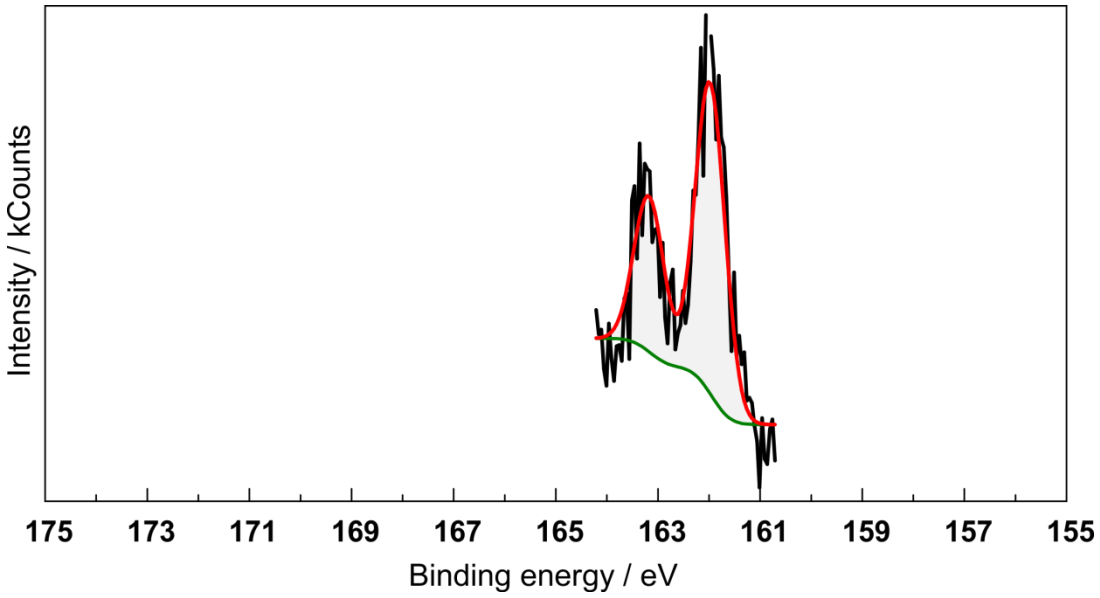


Figure S 11. S 2p XP core level spectrum of AUD (hv = 260 eV).

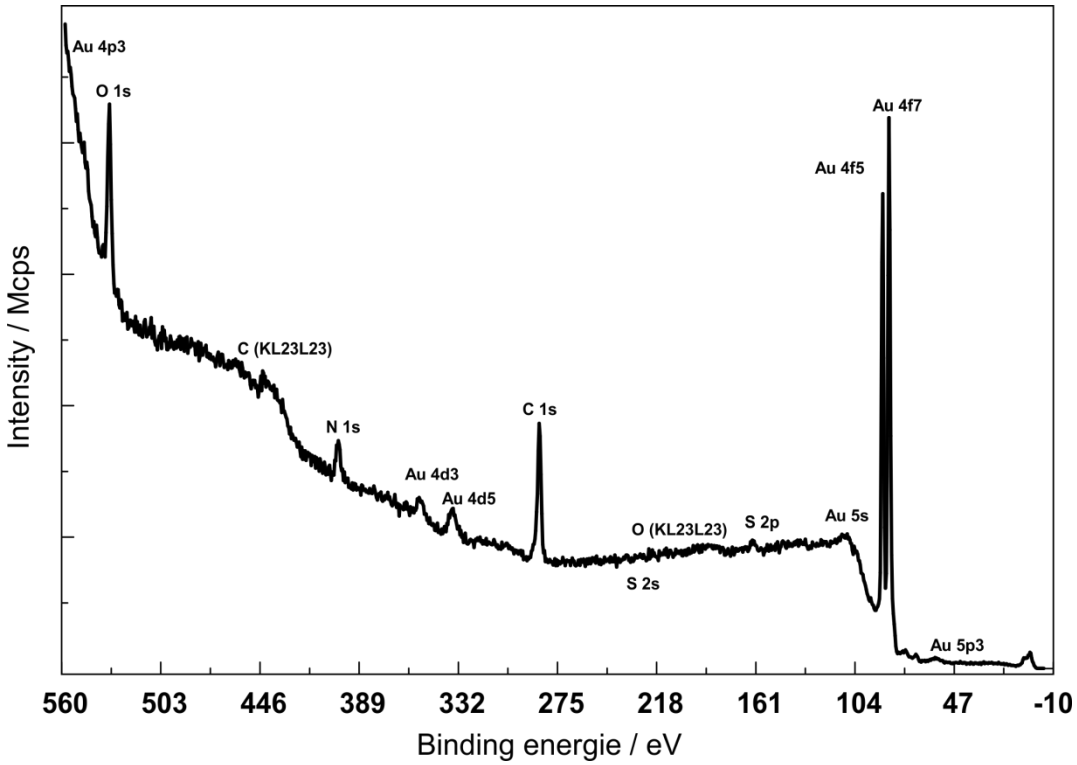


Figure S 12. Survey XP spectrum of HEX clicked to AUD (hv = 700 eV).

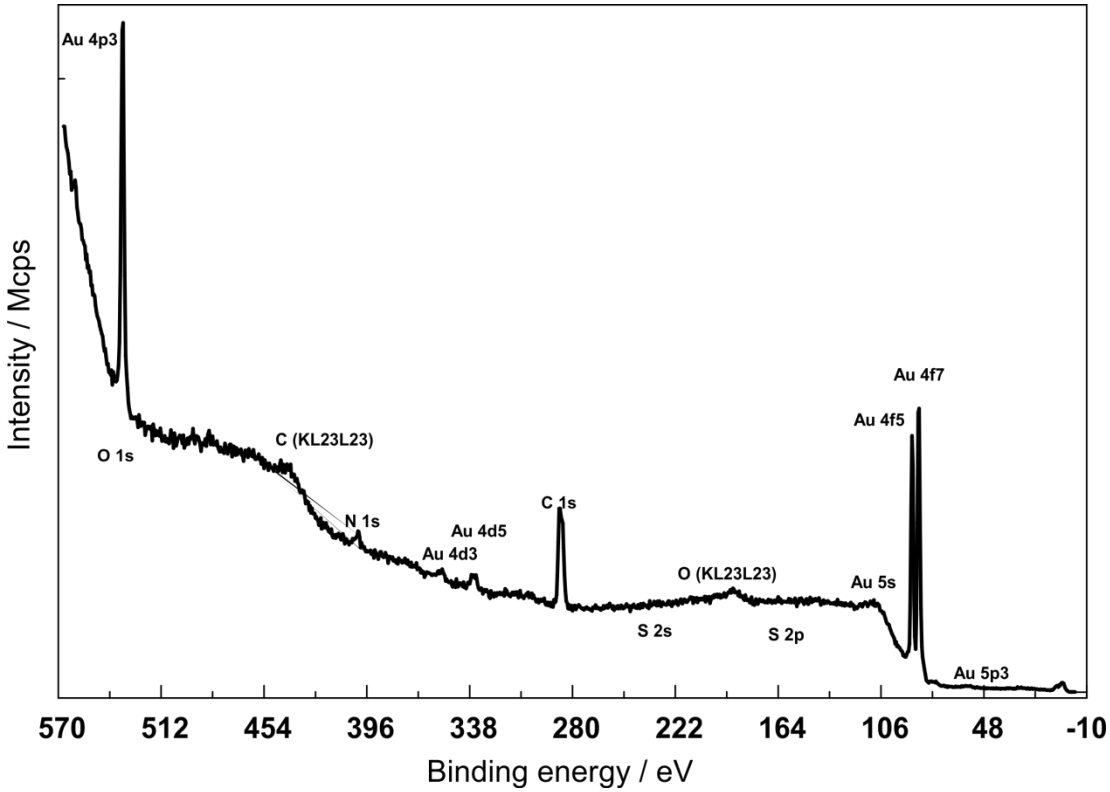


Figure S 13. Survey XP spectrum of CE1 clicked to AUD (hv = 700 eV).

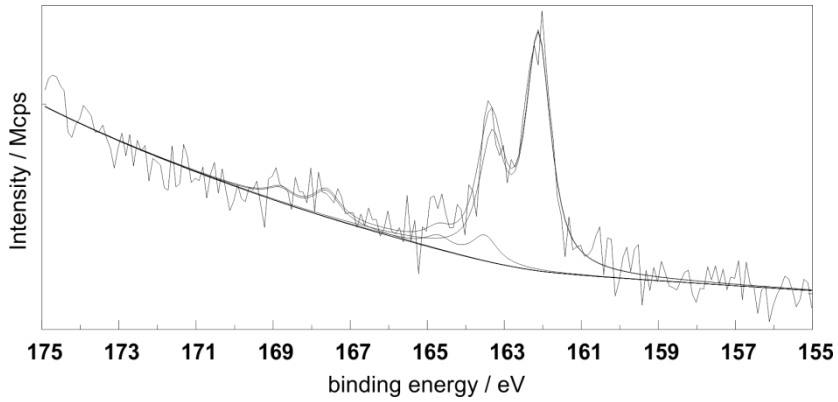


Figure S 14. S 2p core level spectrum of CE1 clicked to AUD (hv = 260 eV).

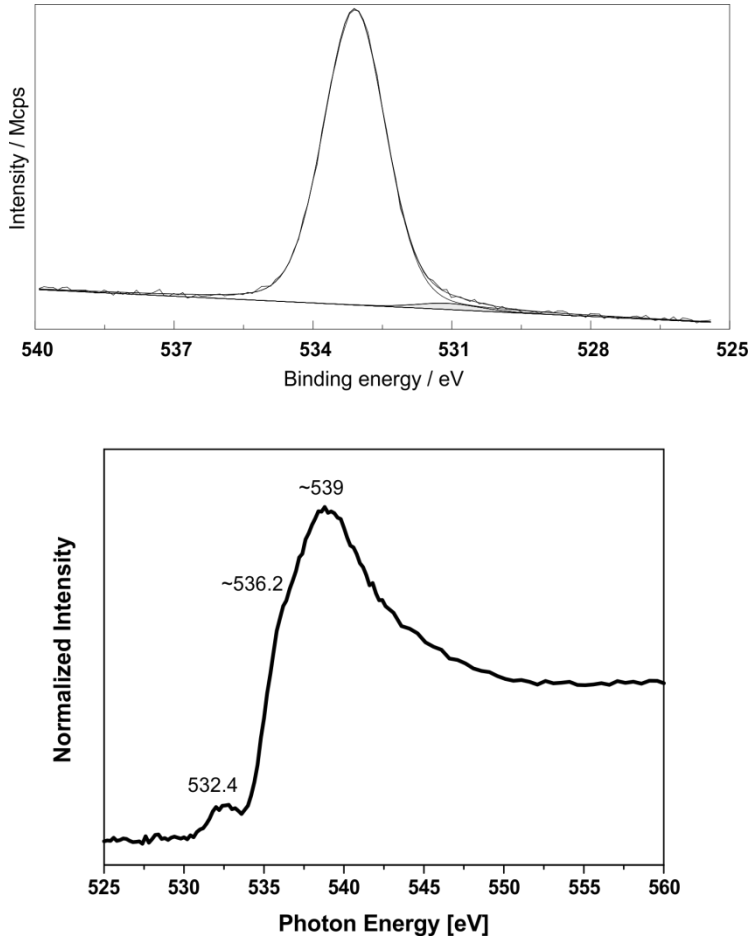


Figure S 15. O 1s core level spectrum (hv = 650 eV) and O K-edge NEXAFS spectrum of CE1 clicked to AUD.

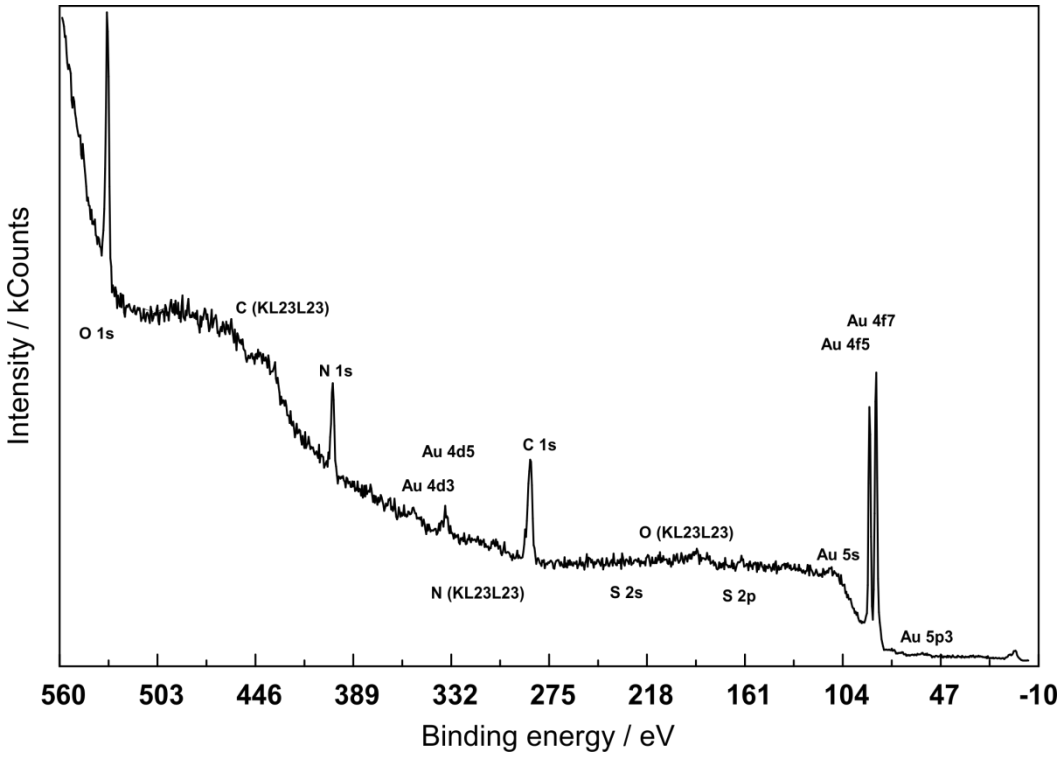


Figure S 16. Survey XP spectrum of DP1 clicked to AUD (hv = 700 eV).

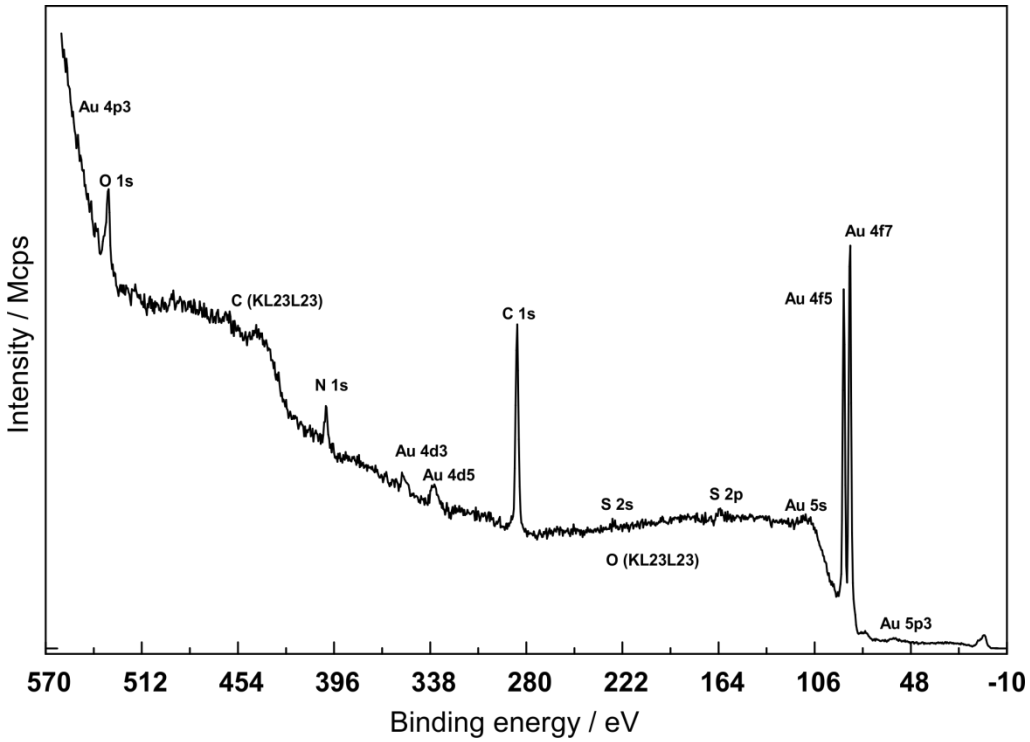


Figure S 17. Survey XP spectrum of TLM1 clicked to AUD (hv = 700 eV).

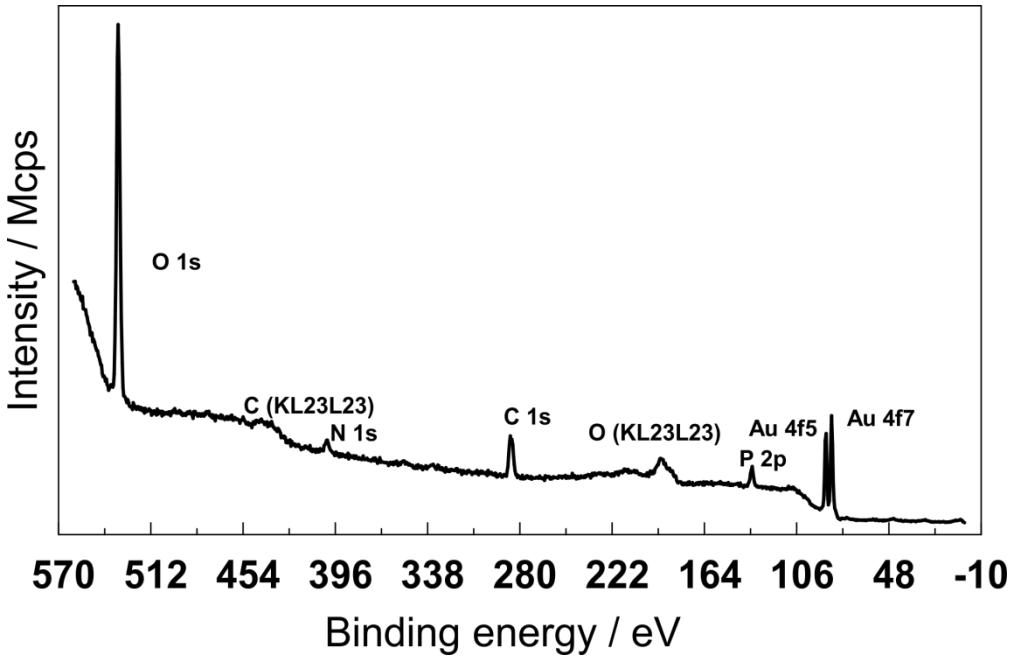


Figure S 18 Survey XP spectrum of CE1 clicked to AUD after adding AM2 (hv = 700 eV).

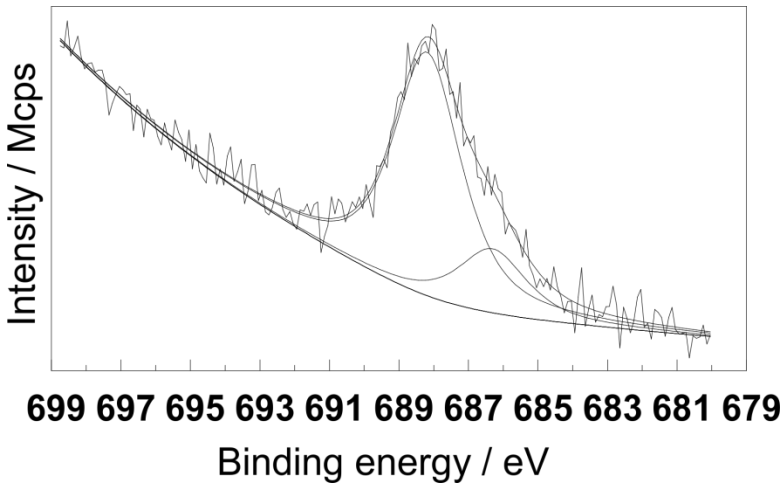


Figure S 19. F 1s core level spectrum of CE1 clicked to AUD after adding AM2 (hv = 780 eV).

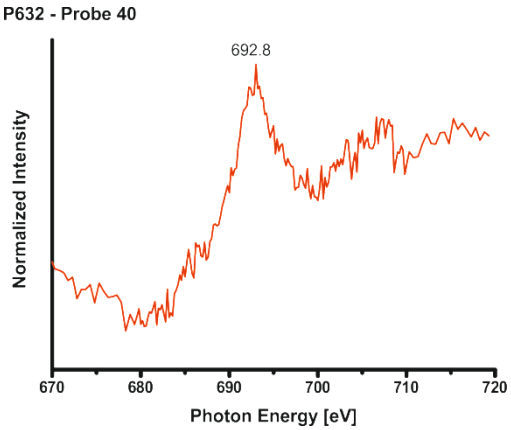


Figure S 20. F K-edge NEXAFS spectrum of CE1 clicked to AUD after adding AM2.

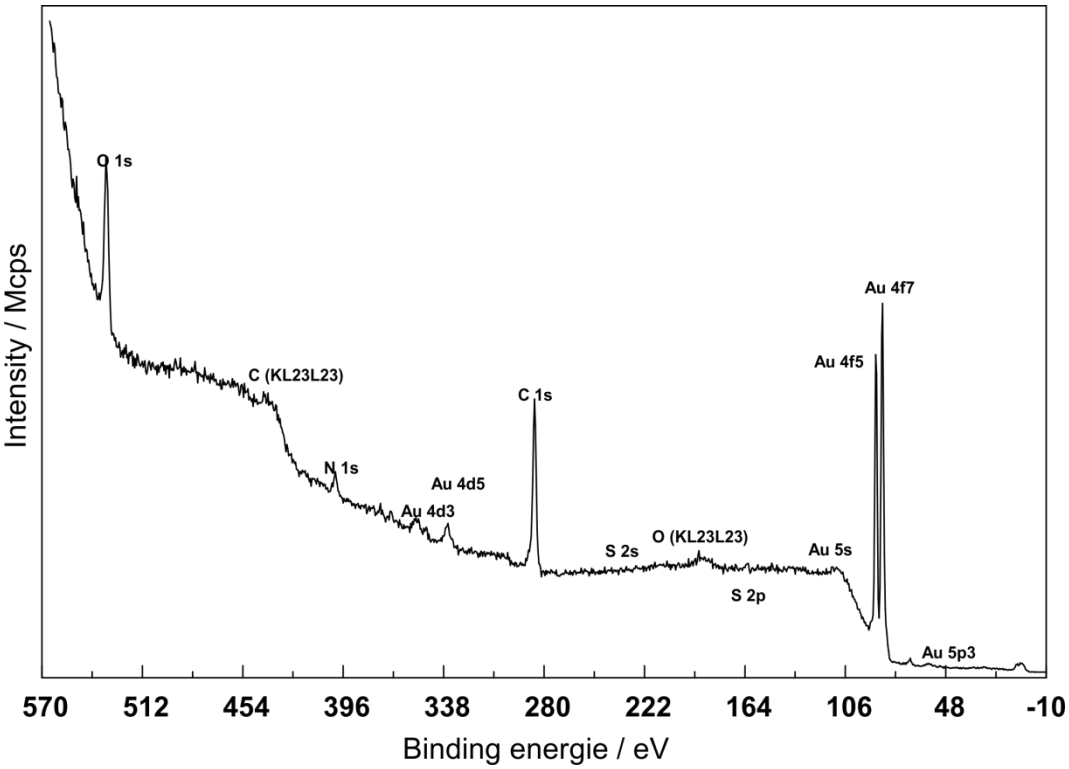


Figure S 21. Survey XP spectrum of DP1 clicked to AUD afrer adding TLM2 (hv = 700 eV).

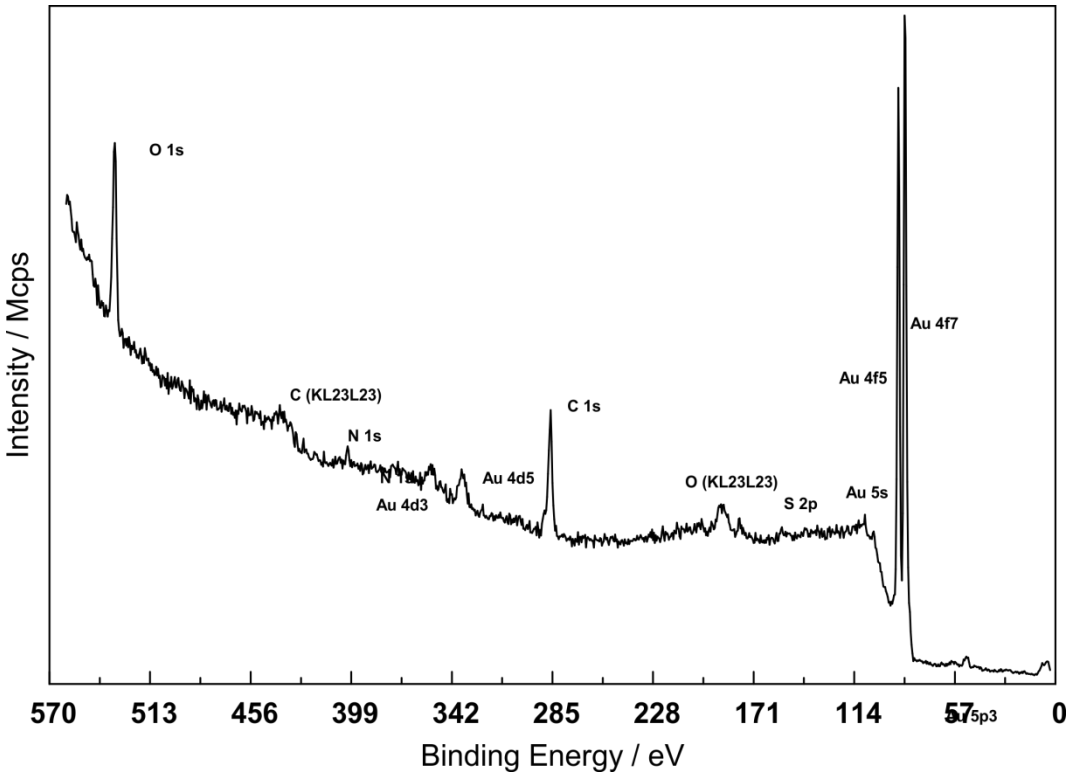


Figure S 22. Survey XP spectrum of TLM1 clicked to AUD after adding DP2 (hv = 700 eV).

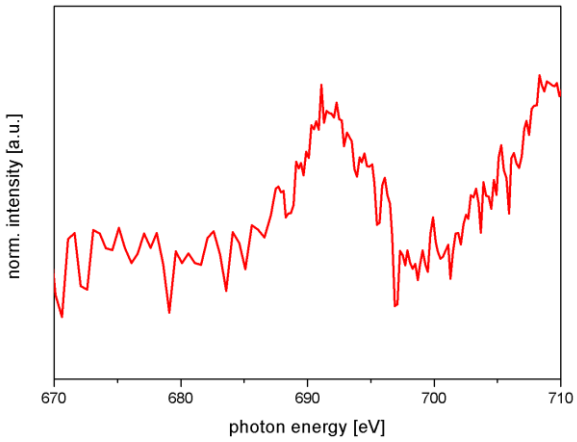


Figure S 23. . F K-edge NEXAFS spectrum of TLM1 clicked to AUD after adding DP2.

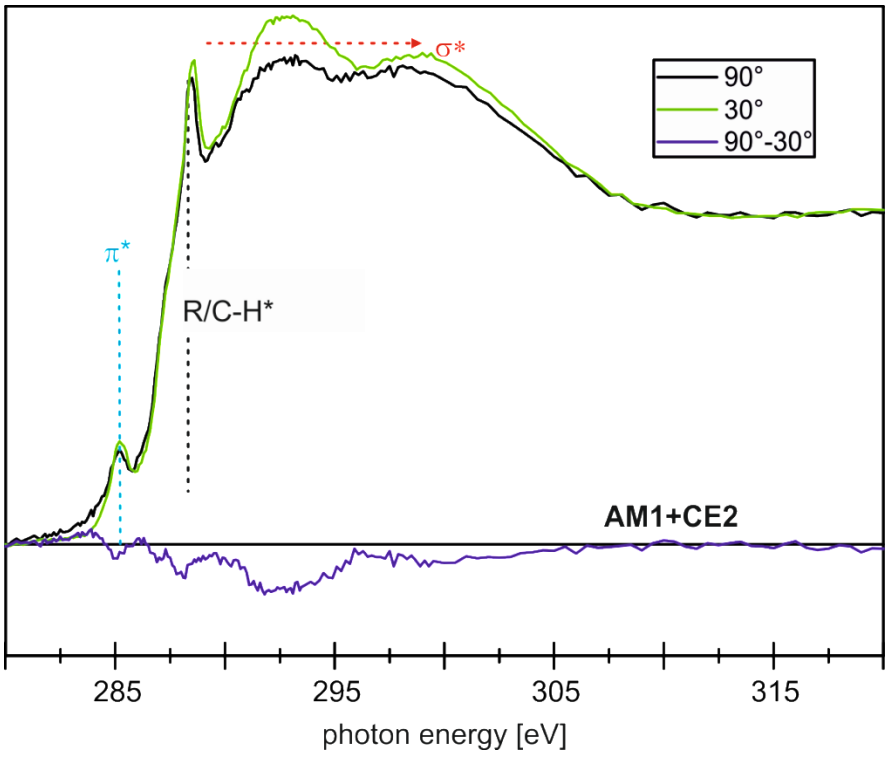


Figure S 24. Angle-resolved C K-edge NEXFAS of AM1 clicked to the surface after immersion in CE2 solution.

References

1. ISO15472:2010, 2010.
2. K. Heister, M. Zharnikov, M. Grunze, L. S. O. Johansson and A. Ulman, *Langmuir*, 2000, **17**, 8-11.
3. J. Stöhr, *NEXAFS Spectroscopy*, Springer, Heidelberg, Germany, 1992.
4. B. L. Alford and H. M. Hugel, *Org. Biomol. Chem.*, 2013, **11**, 2724-2727.