Supporting Information

Absolute Configuration Determination using Enantiomeric Pairs of Molecularly Imprinted Polymers

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Experimentals

N,O-bismethacryloyl ethanolamine (NOBE, S1) crosslinking monomer synthesis. In a 500 mL roundbottom, ethanolamine (4.017 g, 0.0658 mol) and 225 mL DCM were cooled to 0℃. 4-Dimethylaminopyridine (1.6374 g, 0.0134 mol) was added to the solution followed by the addition of methacrylic acid (12.6523 g, 0.147 mol). N,N'-dicyclohexylcarbodiimide (29.1370 g, 0.141 mol) was added after the solution equilibrated for 5 minutes. The mixture was slowly warmed to room temperature and stirred for 2 days. The DCU was filtered off by vacuum filtration and the organic solution was washed with 1 N HCl (aq) (3 x 100 mL) and sat. $NaHCO_3$ (aq) (7 x 100 mL.) The organic layer was dried over $MgSO_4$ and the solvent evaporated to yield an oil 12.7621 g, 98.4% yield. ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 6.41 (1H, br, NH), 6.06 (1H, s), 5.64 (1H, s), 5.54 (1H, s), 5.27-5.25 (1H, d, J= 8 Hz), 4.25-4.22 (2H, t, J= 6 Hz), 3.58-3.54 (2H, q), 1.90 (3H, s), 1.88 (3H, s.) ^{13}C NMR ($CDCl_3$, 100MHz) δ ppm 168.46, 167.65, 139.78, 135.94, 126.20, 119.76, 63.36, 39.22, 18.58, 18.29.

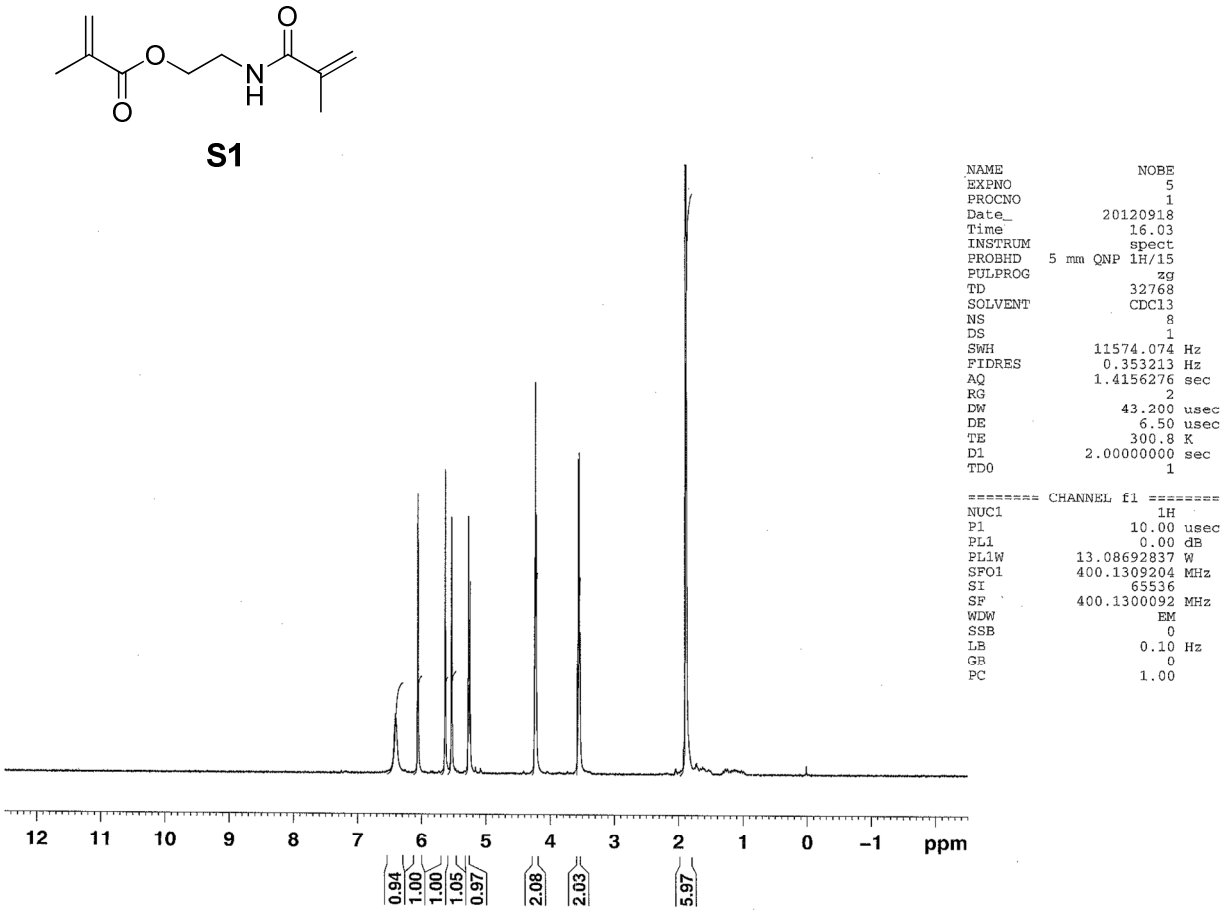


Figure S1. N,O-bismethacryloyl ethanolamine (NOBE, **S1**) ^{1}H NMR

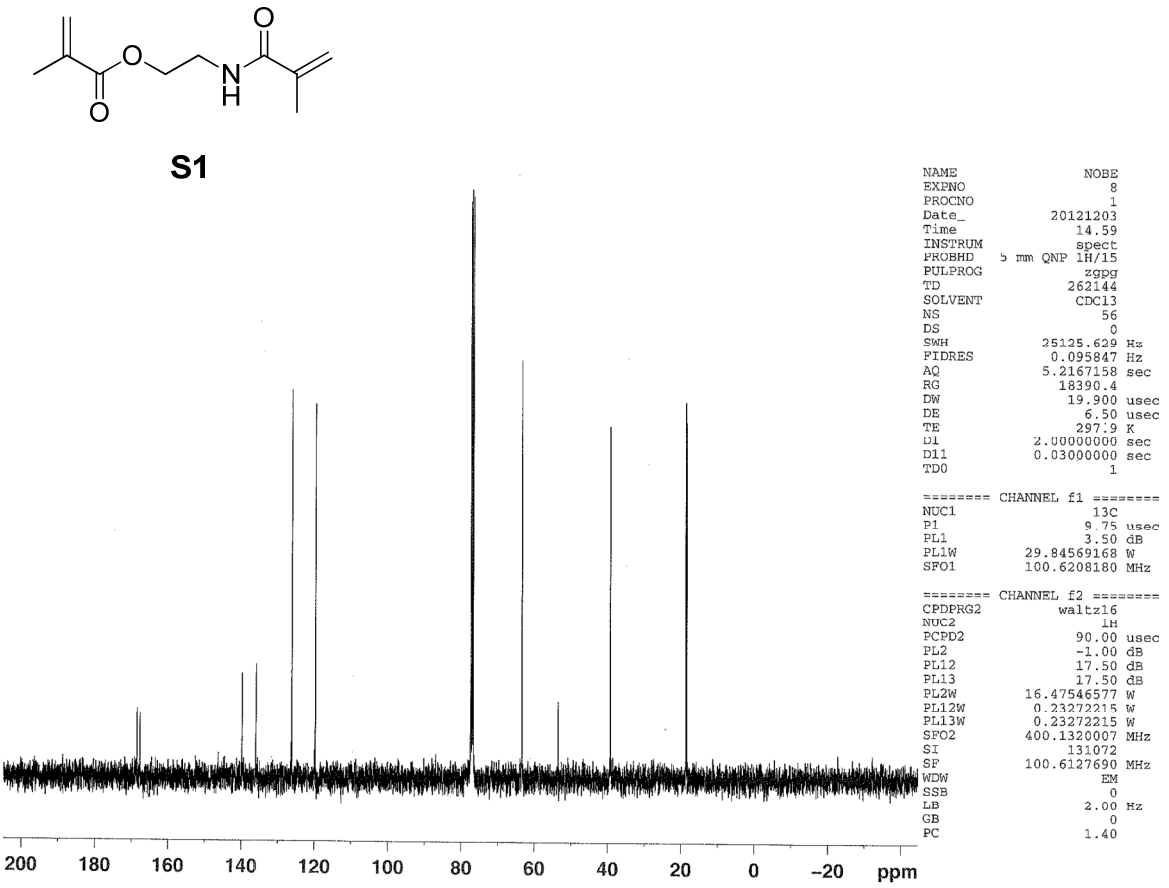
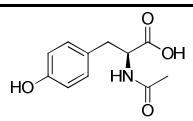
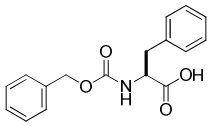
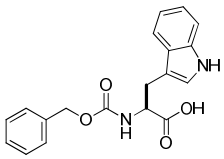
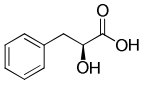
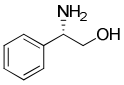
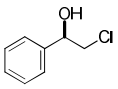
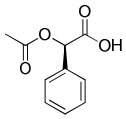
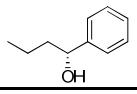
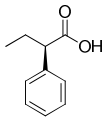
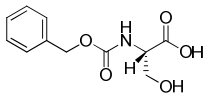


Figure 2. N,O-bismethacryloyl ethanolamine (NOBE, **S1**) ^{13}C NMR

DuoMIP Polymer Formulation and Synthesis. NOBE (3 g) was added to a solution of R or S-tBOC-Tyr (5%[a] or 20%[b] template) dissolved in 3 mL acetonitrile. AIBN (1%) was added to the solution and this was placed into a 13x100 mm glass tube. Nitrogen was used to purge each sample for 5 minutes. After the sample was purged, the tube was capped and Teflon tape and Parafilm were used to seal the system. The tube was then inserted into a photoreactor apparatus where it was submerged in a H_2O bath to maintain the temperature and was exposed to a 450 W mercury arc lamp surrounded by a borosilicate jacket for 8 hours. The polymer was then broken out of the tube and the template was removed by Soxhlet extraction using methanol for 2 days. The polymers were then ground and sized to 25-37 µm. The sized polymer was then packed into 100 x 2.1 mm stainless steel columns and their ability to determine absolute configuration were analyzed by HPLC.

Table S1. Table of γ factors and k' values for absolute configuration determination of several analytes using 5%[a] or 20%[b] of R or S-tBOC-Tyr as the template.[*]

entry	Analytes		k'[a] on S	k'[a] on R	γ[a]	k'[b] on S	k'[b] on R	γ[b]
1		S	-	-	-	11.2	6.5	1.7
2		S	0.9[c]	0.6[c]	NA[c]	1.9	1.5	1.3
3		R	0.6[c]	0.7[c]	NA[c]	1.6	2.3	1.4
4		S	1.6	1.2	1.3	4.0	3.0	1.3
5		R	1.4	1.4	1.0[d]	3.0	3.7	1.2
6		S	0.9[c]	0.7[c]	NA[c]	1.8	1.4	1.3
7		S	4.0	2.2	1.8	5.1	3.2	1.6
8		S	0.1[c]	0.1[c]	NA[c]	0.2[c]	0.1[c]	NA[c]
9		R	0.1[c]	0.1[c]	NA[c]	0.2[c]	0.1[c]	NA[c]
10		R	-	-	-	0.8[c]	0.8[c]	NA[c]
11		R	0.1[c]	0.1[c]	NA[c]	0.2[c]	0.1[c]	NA[c]
12		S	0.3[c]	0.3[c]	NA[c]	0.5[c]	0.5[c]	NA[c]
13		R	0.4[c]	0.3[c]	NA[c]	0.5[c]	0.5[c]	NA[c]
14		S	1.5	1.3	1.2	2.7	2.5	1.1[d]
15		R	1.5	1.3	1.2	2.7	2.5	1.1[d]

[*]HPLC conditions: particle size, 25-37 μm; column size, 100x2.1 mm; flow rate: 0.1 mL/min; mobile phase: 99/1 (MeCN/AcOH); injected volume: 5 μL; wavelength detection: 260 nm[a]; analyte concentrations: 0.2 mM (entries 4-5)[a and b], 1 mM (entries 1-3, 6-7, 10-11, 14-15)[a], 2 mM (entries 12-13)[a], 5 mM (entries 8-9)[a] and 1 mM/262 nm (entries 2-3)[b], 1 mM/262 nm (entries 6, 11)[b], 2 mM/262 nm (entries 12-13)[b], 5 mM/262 nm (entries 2-3, 8-9)[b], 10 mM/262 nm (entry 7)[b]. [c]The k' is lower than minimum allowed by criteria and cannot be used to calculate the γ factor for AC. [d]The γ factor is lower than minimum allowed by criteria and cannot be used for AC.

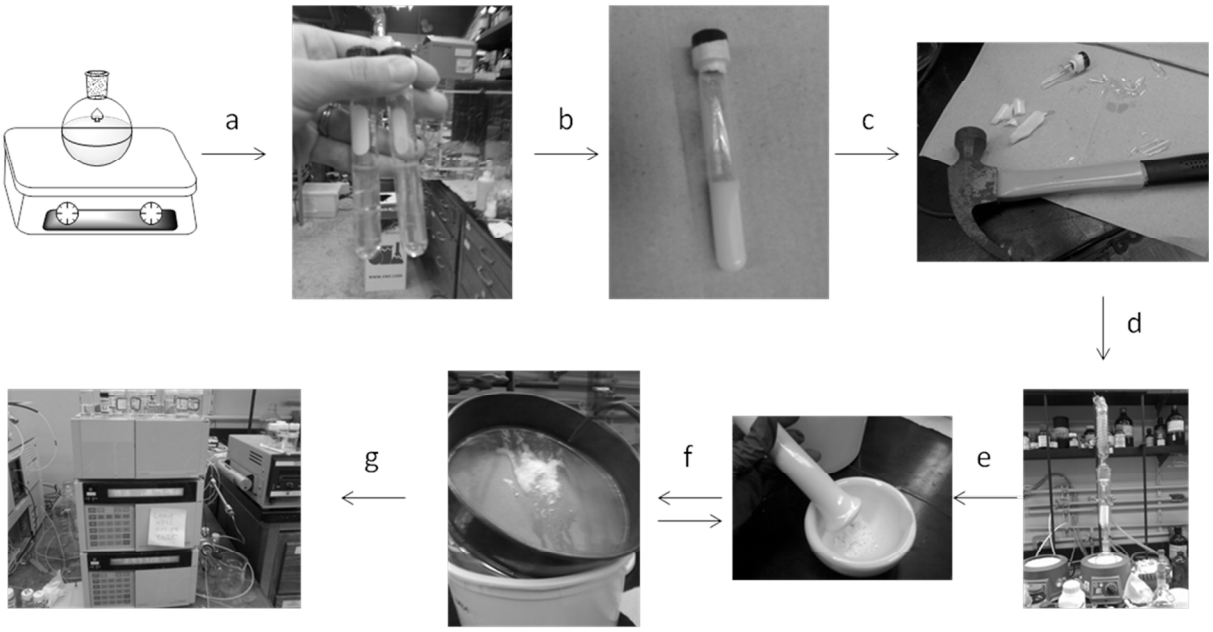


Figure S3. Step by step pictorial of the polymer synthesis grinding, and packed column.

a) Combine synthesized crosslinking monomer with template in solution, add initiator and polymerize.

b) The MIP formed will be a solid polymer.

c) Break the polymer out of the tube.

d) Put the polymer in a soxhlet extractor to remove the template.

e) After template removal, grind the polymer to the desired particle size.

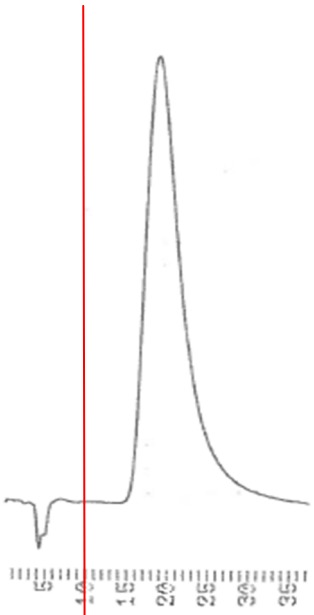
f) Wash and grind more polymer until enough material is acquired to pack the HPLC.

g) Put the column packed with imprinted polymer onto the HPLC for analysis.

Chromatograms. The following figures compare the chromatograms of selected analytes from the list in Table 1 on the DuoMIPs. In some cases, the chromatograms were analyzed at different chart speeds making them appear to be different sizes; however, all chromatograms were normalized in size with respect to time and calibrated to the red line.

Figure S4. S-BOC-Tyr on the DuoMIPs

2.5 mM S-BOC-Tyr on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



2.5 mM S-BOC-Tyr on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

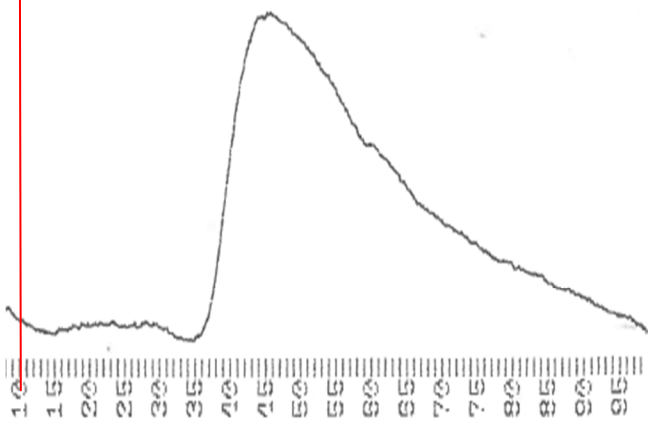
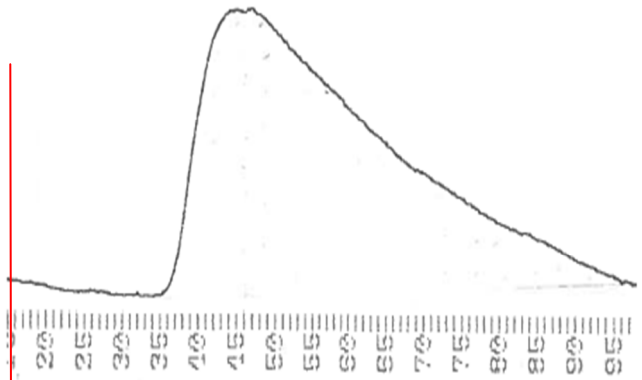


Figure S5. R-BOC-Tyr on the DuoMIPs

2.5 mM R-BOC-Tyr on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



2.5 mM R-BOC-Tyr on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

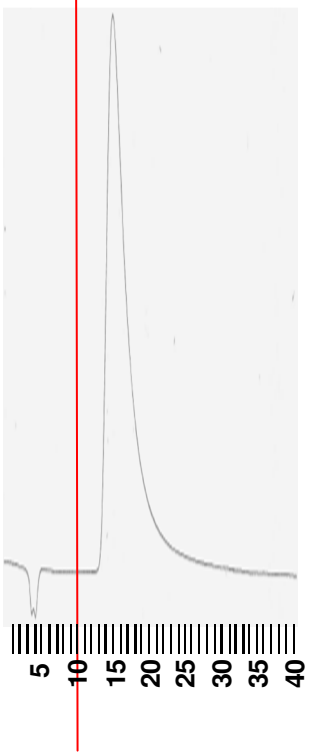
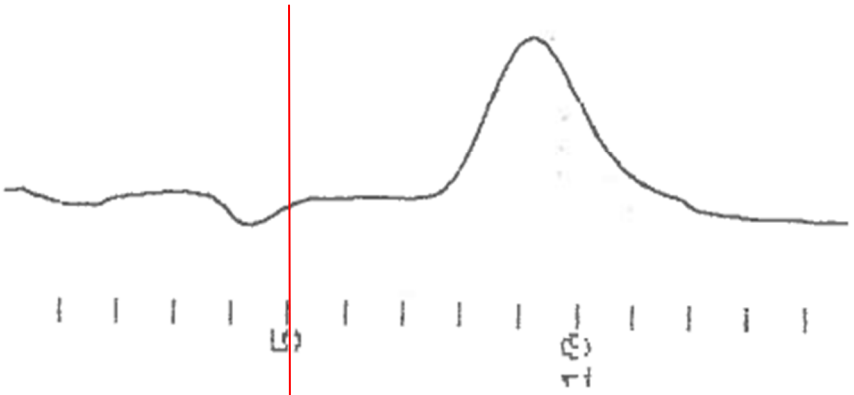


Figure S6. S-Z-Phe (Table S1, entry 2) on the DuoMIPs

IMPORTANT NOTE: Although the retention time on the R-MIP is higher, the k' of the analyte on the S-MIP is higher, as shown in Table 1. This is due to the difference in dead volume values. Thus, AC is still accurately accounted for.

1 mM S-Z-Phe (Table S1, entry 2) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



1 mM S-Z-Phe (Table S1, entry 2) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

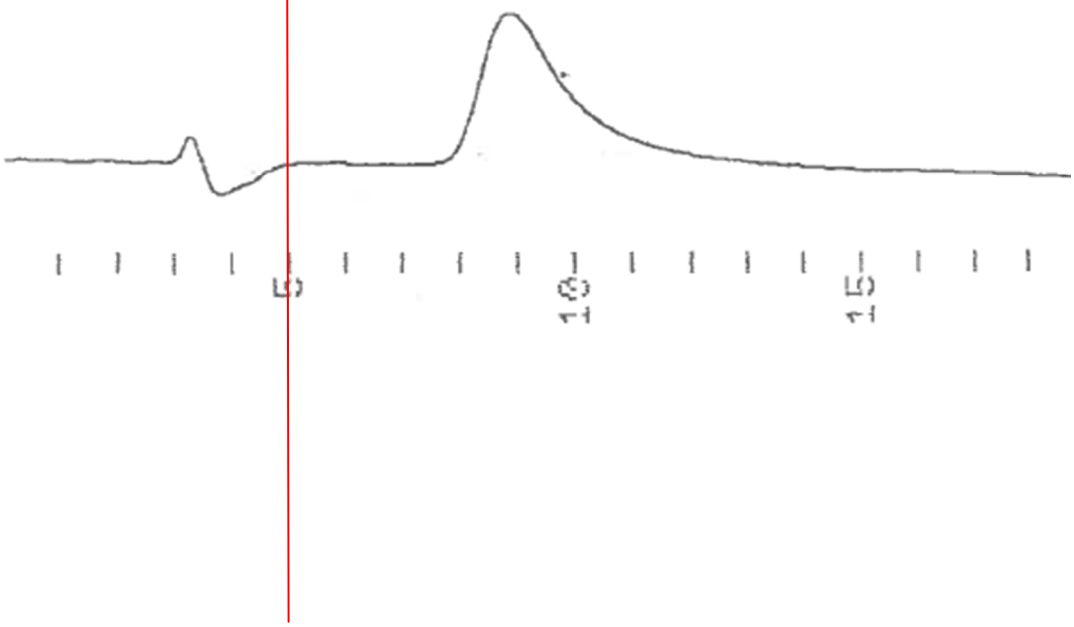
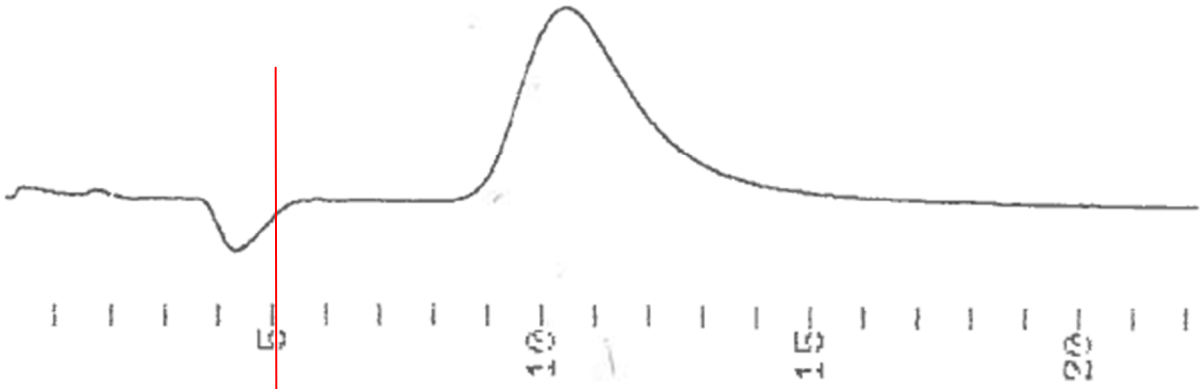


Figure S7. R-Z-Phe (Table S1, entry 3) on the DuoMIPs

1 mM R-Z-Phe (Table S1, entry 3) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



1 mM R-Z-Phe (Table S1, entry 3) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

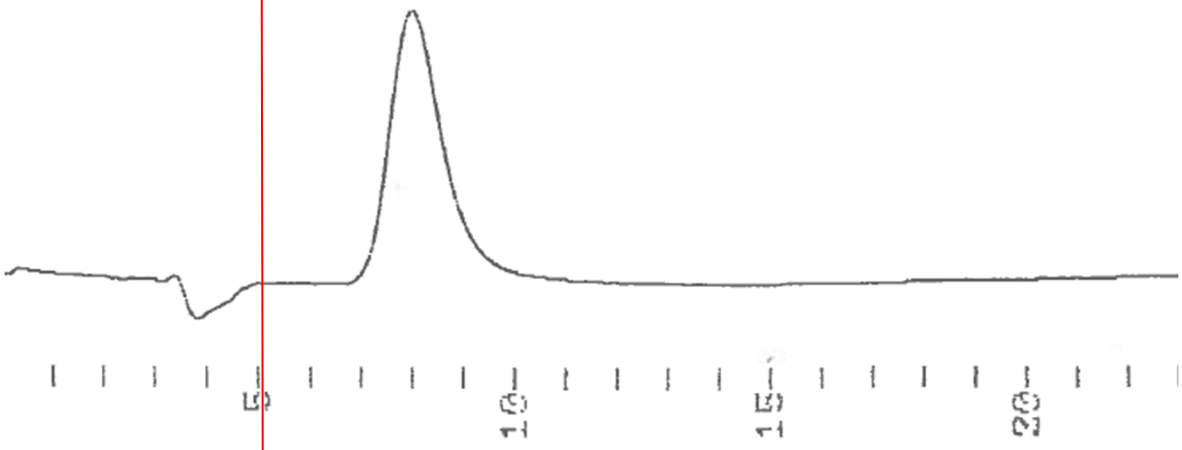
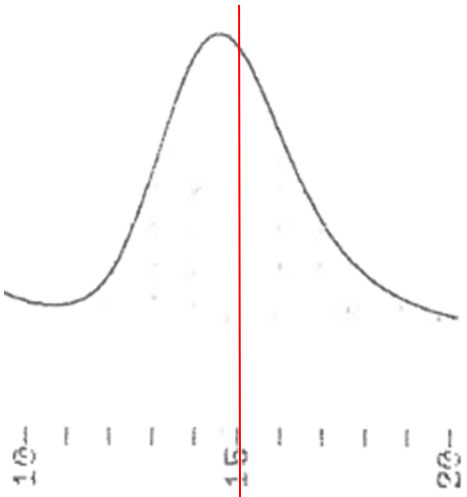


Figure S8. S-Z-Trp (Table S1, entry 4) on the DuoMIPs

0.2 mM S-Z-Trp (Table S1, entry 4) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



0.2 mM S-Z-Trp (Table S1, entry 4) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

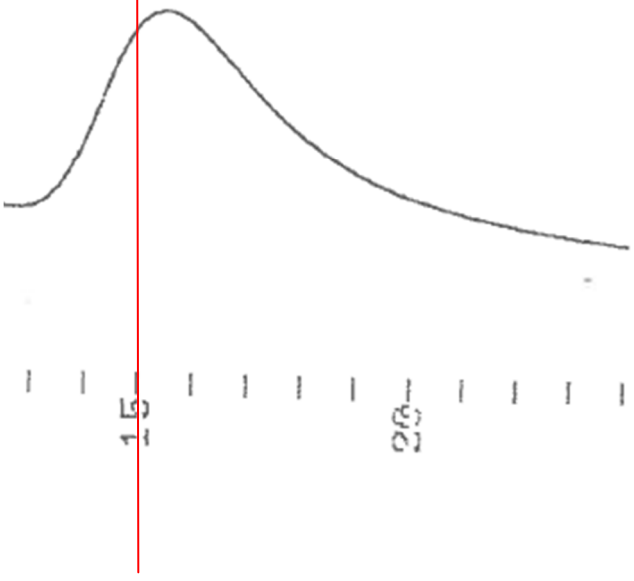
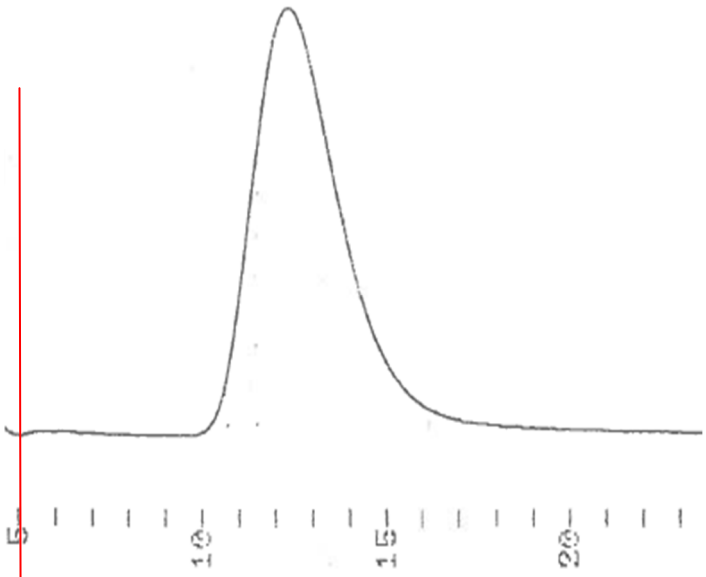


Figure S9. S-Z-Ser (Table S1, entry 14) on the DuoMIPs

IMPORTANT NOTE: Although the retention time on the R-MIP is higher, the k' values of the analyte on both DuoMIPs are the same, as shown in Table 1. This is due to the difference in dead volume values. Thus, AC cannot be determined for this analyte.

1 mM S-Z-Ser (Table S1, entry 14) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



1 mM S-Z-Ser (Table S1, entry 14) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

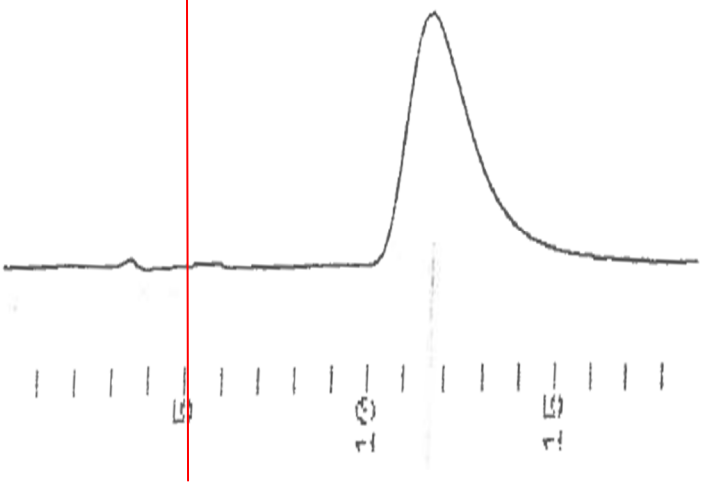
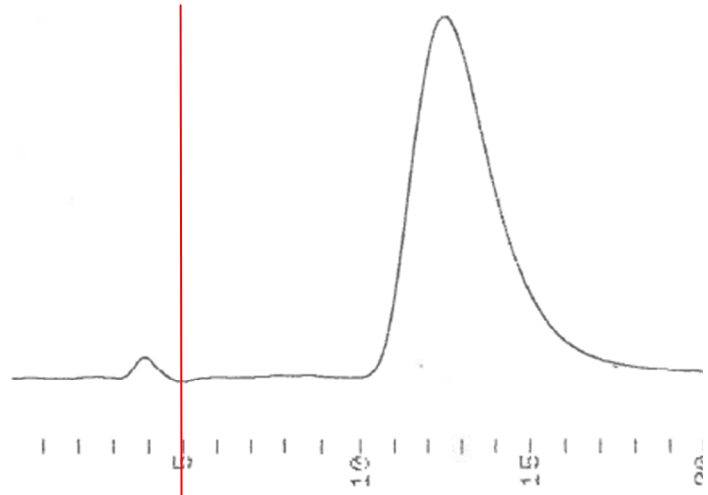


Figure S10. R-Z-Ser (Table S1, entry 15) on the DuoMIPs

IMPORTANT NOTE: Although the retention time on the R-MIP is higher, the k' values of the analyte on both DuoMIPs are the same, as shown in Table 1. This is due to the difference in dead volume values. Thus, AC cannot be determined for this analyte.

1 mM R-Z-Ser (Table S1, entry 15) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



1 mM R-Z-Ser (Table S1, entry 15) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

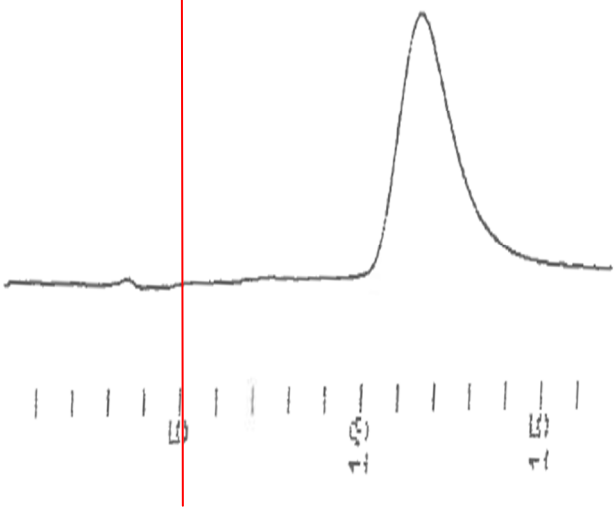
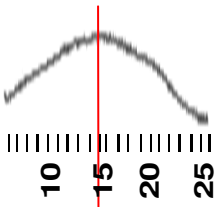


Figure S11. S-phenyl glycinol (Table S1, entry 7) on the DuoMIPs

1.0 mM S-phenyl-glycinol (Table S1, entry 7) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



1.0 mM S-phenyl-glycinol (Table S1, entry 7) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

23)

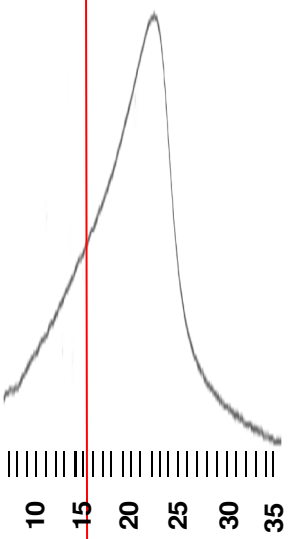
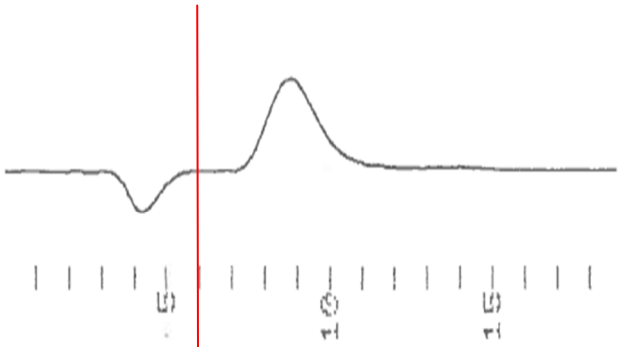


Figure S12. S-phenyl lactic acid (Table S1, entry 6) on the DuoMIPs

IMPORTANT NOTE: Although the retention time on the R-MIP is higher, the k' of the analyte on the S-MIP is higher, as shown in Table 1. This is due to the difference in dead volume values. Thus, AC is still accurately accounted for.

1 mM S-phenyl lactic acid (Table S1, entry 6) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



1 mM S-phenyl lactic acid (Table S1, entry 6) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

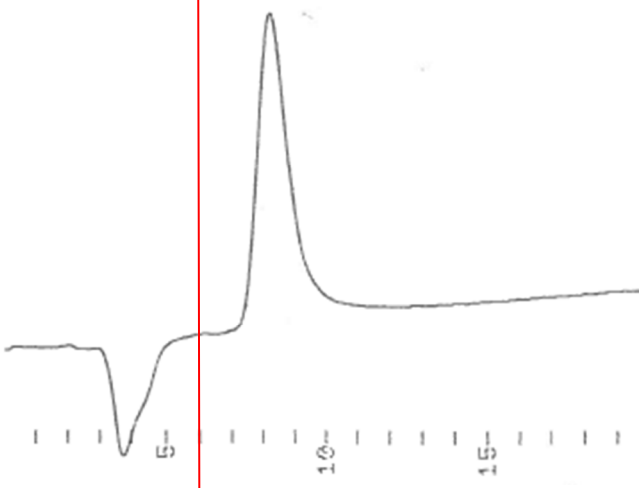
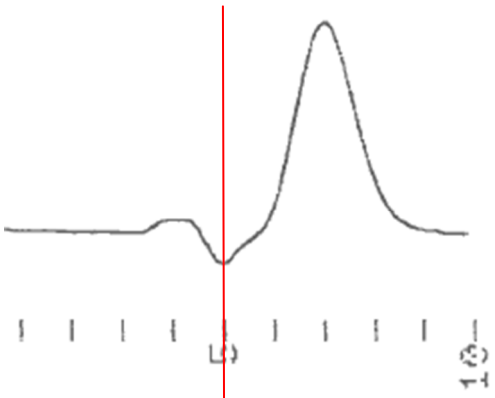


Figure S13. R-acetyl mandelic acid (Table S1, entry 10) on the DuoMIPs

IMPORTANT NOTE: Although the retention time on the R-MIP is higher, the k' values for the R-acetyl madelic acid on both DuoMIPs are the same, as shown in Table 1. This is due to the difference in dead volume values. Thus, AC cannot be determined for this analyte.

1 mM R-acetyl mandelic acid (Table S1, entry 10) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



1 mM R-acetyl mandelic acid (Table S1, entry 10) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

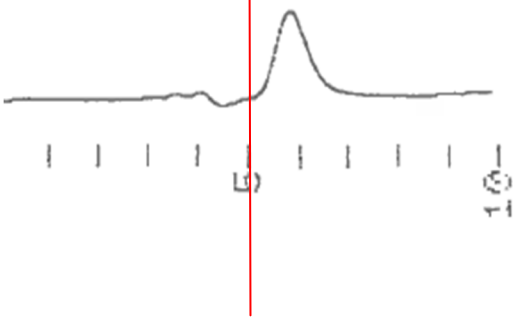
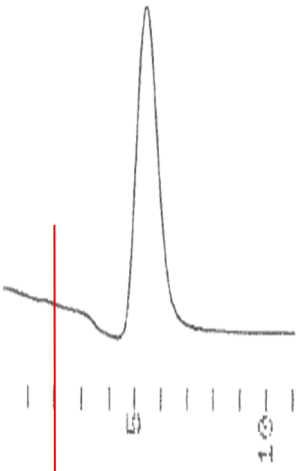


Figure S14. S-phenyl butyric acid (Table S1, entry 12) on the DuoMIPs

IMPORTANT NOTE: Although the retention time on the R-MIP is higher, the k' values of the analyte on both DuoMIPs are the same, as shown in Table 1. This is due to the difference in dead volume values. Thus, AC cannot be determined for this analyte.

2 mM S-phenyl butyric acid (Table S1, entry 12) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



2 mM S-phenyl butyric acid (Table S1, entry 12) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

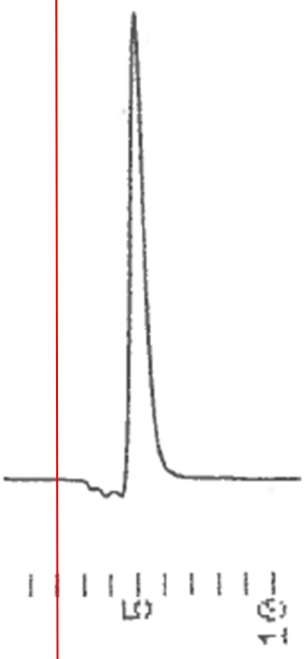
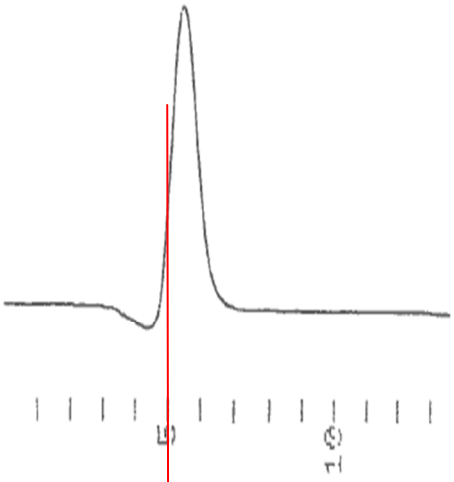


Figure S15. R-phenyl butyric acid (Table S1, entry 13) on the DuoMIPs

IMPORTANT NOTE: Although the retention time on the R-MIP is higher, the k' values of the analyte on both DuoMIPs are the same, as shown in Table 1. This is due to the difference in dead volume values. Thus, AC cannot be determined for this analyte.

2 mM R-phenyl butyric acid (Table S1, entry 13) on the 20% R-BOC-Tyr imprinted column (D_v = 3.61)



2 mM R-phenyl butyric acid (Table S1, entry 13) on the 20% S-BOC-Tyr imprinted column (D_v = 3.23)

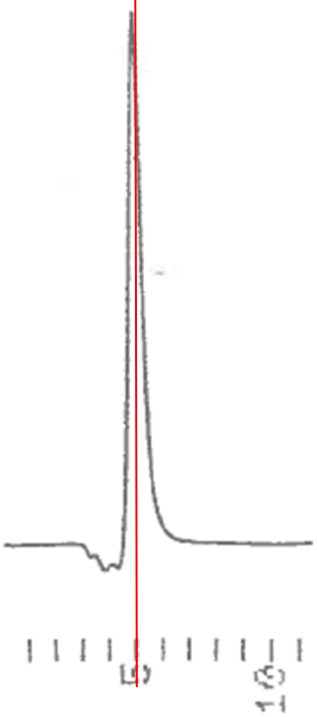


Figure S16. S-phenyl glycinol (Table S1, entry 7) depicted fitting in the S-MIP binding cavity (S16a) and S-phenyl glycinol depicted with poor fit in the R-MIP binding cavity (S16b)