Experimental Section

All starting materials were from Aldrich and were used as received unless otherwise stated. TentaGel resin was obtained from RAPP Polymere. ^{1}H NMR spectra at 300 MHz NMR spectra and ^{13}C NMR spectra at 75.4 MHz were recorded with the solvent proton signal as the reference. ^{19}F NMR spectra at 282.25 MHz were recorded with trifluoroacetic acid fluorine signal as the reference. Analytical HPLC was performed on a Beckman system with a reversed phase C_{18} column, UV detection at 220 nm and H_2O/Acetonitrile as the solvent. LC-MS was conducted with an Agilent 1100 Series LC/MSD system, operating electrospray ionization in either positive or negative mode. GC-MS was performed on an Agilent 6890 GC system with an Agilent 5973 Network Mass Selective Detector. Preparative TLC was performed on Aldrich silica gel GF plates (1000 μm thick). Baker Silica Gel (40 μm) was used for flash chromatography.

Acid (4). At 0 ^{o}C, to a stirring solution containing ethyl vinylether (600 mg, 8.3 mmol), $NaHCO_3$ (680 mg, 8.0 mmol), and commercial tetrafluoro-2-(tetrafluoro-2-iodoethoxy)ethanesulfonyl fluoride (3.5 g, 8.0 mmol) in CH_3CN (8 mL) and H_2O (7 mL) was slowly added $Na_2S_2O_4$ (1.4 g, 8.0 mmol). The reaction mixture was stirred at 5 ^{o}C for 50 min. The pH of the reaction mixture was adjusted to 6.2~7.0 by adding 3.0 N aqueous HCl and the mixture stirred at 25 ^{o}C for another 20 min. The reaction mixture was extracted with CH_2Cl_2, washed with water and concentrated under reduced pressure. The oily residue was dissolved in acetone (38 mL) and the solution was added to a stirring mixture of 2-methyl-butene-2 (36 mL), NaH_2PO_4 (4.0 g, 30 mmol), $NaClO_2$ (5.0 g, 55 mmol) and water (40 mL) at 0-5 ^{o}C. The reaction mixture was stirred at 10-15 ^{o}C for 2 h. The reaction mixture was concentrated under reduced pressure, extracted with ether, washed with brine, dried ($MgSO_4$) and concentrated. The oily crude product was purified on a SiO_2 column (MeOH/$CHCl_3$, 2:98) to give 1.8 g (62%) of the linker as thick oil. ^{1}H NMR ($CDCl_3$, δ): 3.17 (t, *J*=16.8 Hz, $CF_2CH_2CO_2H$), 8.7 (b, CO_2H); ^{13}C NMR ($CDCl_3$, δ): 169.54, 36.69, 36.39, 36.09; ^{19}F NMR ($CDCl_3$, δ): 121.61 (SO_2F), -6.08, -11.51, -36.14, -39.76; MS (ESI) calcd for $C_6H_3F_9O_5S$ 357.96, found: 357.0 $(M-H)^-$, 714.9 $(2M-H)^-$.

Tetrafluoroethanesulfonyl Fluoride Resin (6a). To a stirring solution of the above acid **4** (800 mg, 2.24 mmol) and oxalyl chloride (430 μL, 4.8 mmol) in CH_2Cl_2 (1.6 mL) was

added DMF (one drop). After the evolution of gas, the reaction mixture was stirred for another 1 h and then concentrated under reduced pressure. The oily product was dissolved in CH_2Cl_2 (5 mL), the solution was added to TentaGel NH_2 resin (1.08 g, 0.46 mmol/g loading) and the resin was cooled to ~0 ^{0}C for 10 min. To the resin was slowly added diisopropylethylamine (1.2 mL, 7.0 mmol), and the resin was shaken at room temperature overnight. The beads were washed with CH_2Cl_2 and dried under vacuum overnight to give resin-bound linker **6a**. ^{19}F NMR ($CDCl_3$, δ): 121.43 (SO_2F), -6.27, -11.35, -36.28, -39.47.

General Procedure for Resin Bound Phenol (7). A mixture of phenol (0.68 mmol), K_2CO_3 (100 mg, 0.72 mmol), resin-bound linker **6** (80 mg, 0.034 mmol) and DMF (1.0 mL) was shaken at room temperature overnight. The resin was washed with water, DMF and CH_2Cl_2, and was dried under vacuum overnight to give resin-bound phenol **7**.

General Procedure for the Preparation of Arenes (8a-8l) by Reductive Cleavage of the Resin Bound Phenol (7). To the dry resin **7** were added $Pd(OAc)_2$ (6.0 mg, mmol), 1,3-bis(diphenyl-phosphino)propane (dppp, 16.0 mg, mmol), DMF (1.2-1.4 mL) and a mixture of HCO_2H (180 μL) and Et_3N (460 μL). The mixture was shaken at 85 ^{0}C for 120 min. The polymer beads were filtered and washed with Et_2O. The combined organic phase was washed with aqueous Na_2CO_3 and water, and evaporated to dryness. The residue was dissolved in Et_2O and eluted through a short column of SiO_2 to removed inorganic residues. The crude products were purified by preparative TLC to give the desired products **37** in > 95 % purity.

Meclizine (12). A mixture of 3-methyl-4-hydroxybenzaldehyde (100 mg, 0.72 mmol), K_2CO_3 (100 mg, 0.72 mmol), resin-bound linker **6** (100 mg, 0.043 mmol) and DMF (1.1 mL) was shaken at room temperature overnight. The beads were washed with water, DMF and CH_2Cl_2, and dried under vacuum overnight to give resin **9**. To the dry resin **9** were added 1-(4-chloronenzhydryl)piperazine **10** (128 mg, 0.40 mmol), THF (800 μL), $Na(CN)BH_3$ (1.0 mL) and acetic acid(23 μL). The mixture was shaken at room temperature overnight. The beads were washed with water, DMF and CH_2Cl_2, and dried under vacuum overnight to give resin **11**.

To the above dry resin **11** were added $Pd(OAc)_2$ (8.0 mg, mmol), 1,3-bis(diphenyl-phosphino)propane (dppp, 17.0 mg, mmol), DMF (1.4 mL) and a mixture of HCO_2H (200 μL) and Et_3N (800 μL). The mixture was shaken at 85 ^{0}C for 120 min. The polymer beads were filtered and washed with Et_2O. The combined organic phase was washed with aqueous

Na_2CO_3 solution and water, and evaporated to dryness. The residue was dissolved in Et_2O and eluted through a short column of Al_2O_3 to removed inorganic residues. The crude products were purified by preparative TLC to give the desired products **12** in > 98 % purity. Analytical data of **12** are identical to that of authentic sample obtained from Sigma.

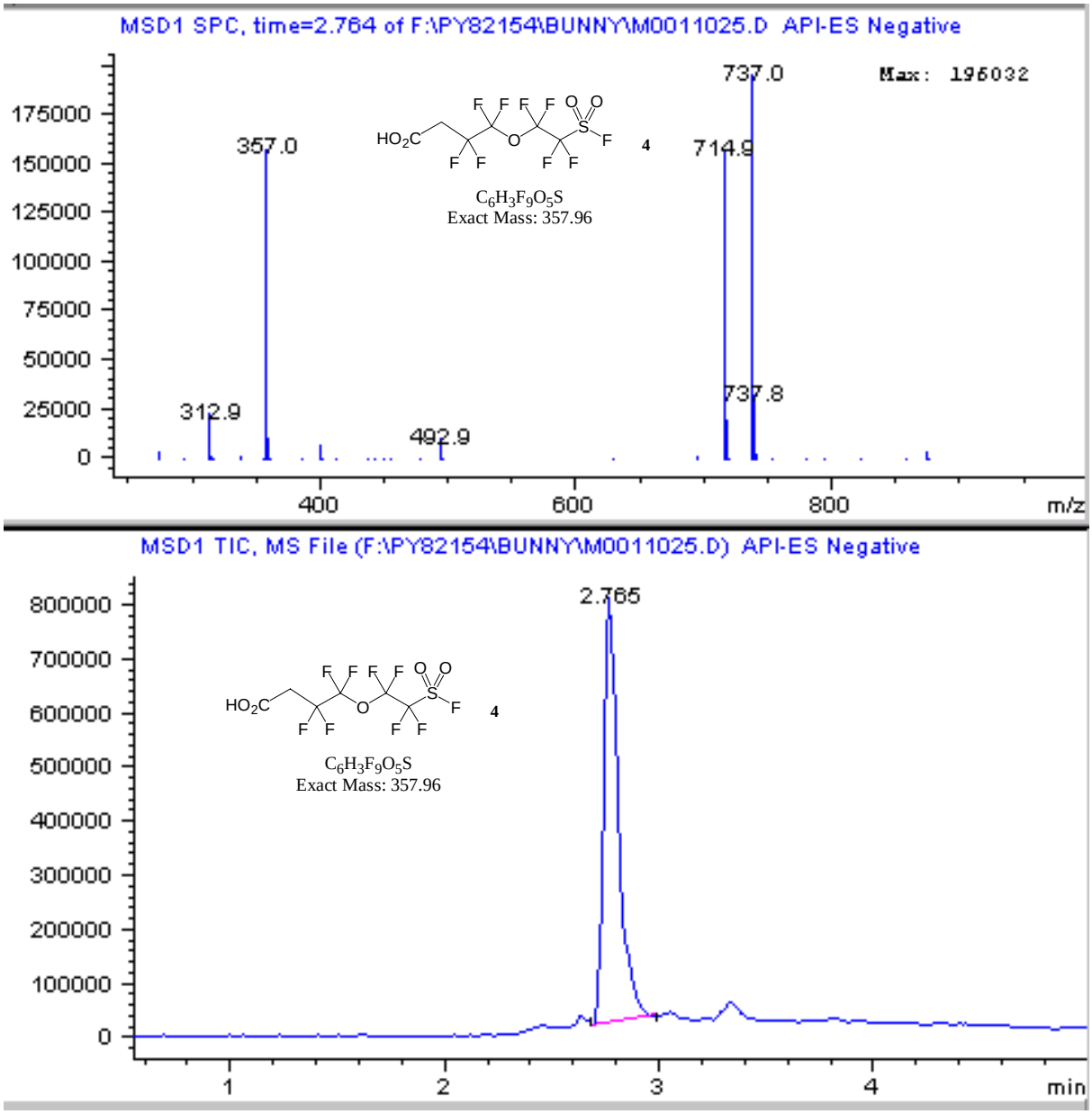

Figure 2. Electrospray ionization mass spectrum (ESIMS) of acid **4** (top) and LC-MS trace of acid **4** (bottom) detected with ESIMS in negative ion mode.

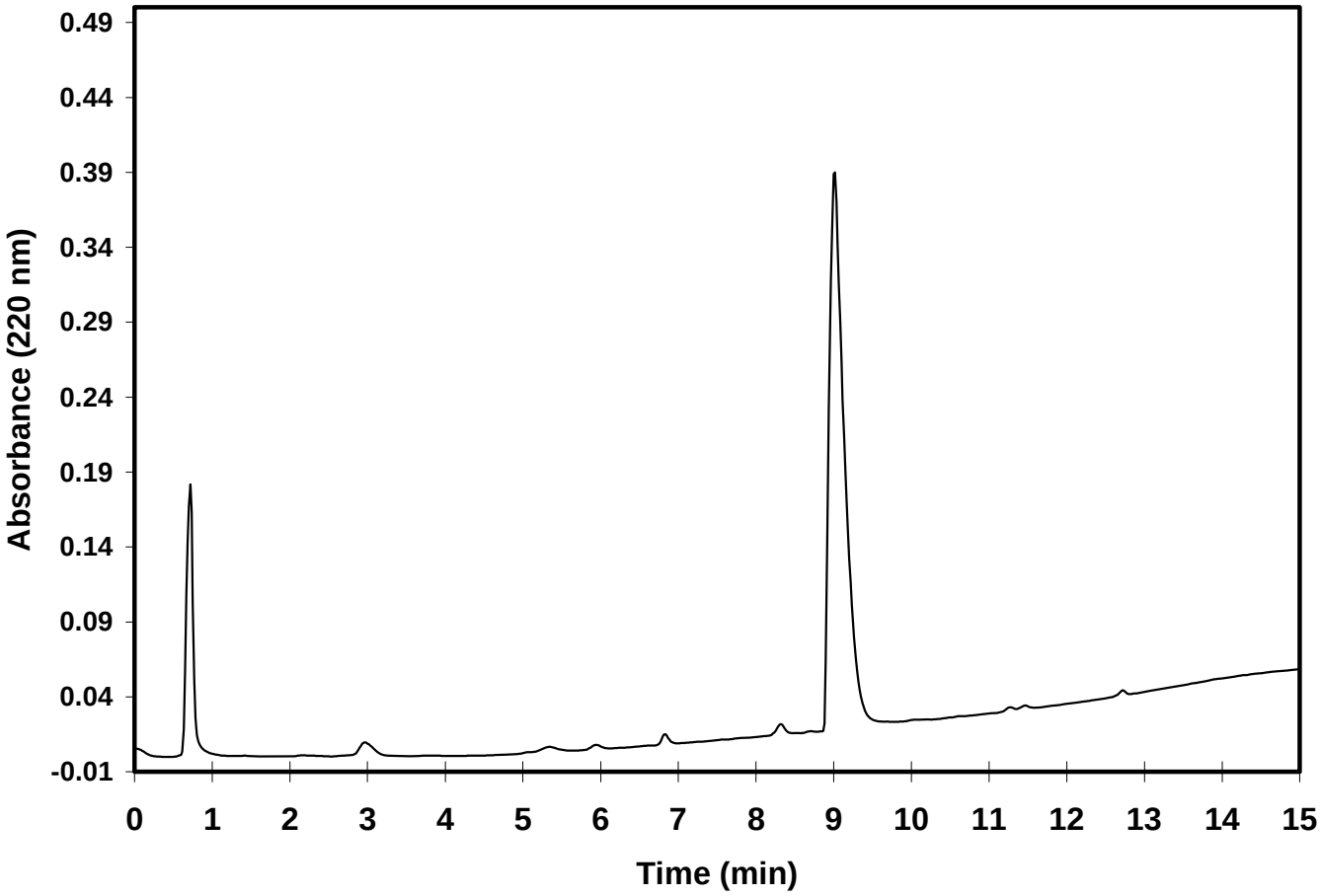

Figure 3. HPLC trace of *Meclizine* **12** after traceless cleavage from the resin.