SUPPLEMENTARY INFORMATION

Single-Step Synthesis of Styryl Phosphonic Acids via Palladium-Catalyzed Heck Coupling of Vinyl Phosphonic Acid with Aryl Halides

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Experimental Methods

All chemicals were used as received without further purification unless noted. Acetonitrile (ACN, ACS) dichloromethane (DCM, ACS), anhydrous tetrahydrofuran (THF, ≥99.9%), N,N-dicyclohexylmethylamine (NCy_2Me, 97%), and anhydrous magnesium sulfate ($MgSO_4$), were obtained from Sigma Aldrich. Sodium hydroxide (NaOH, Pearl 97%) was obtained from Fisher Scientific. Bis(tri-tert-butylphosphine)palladium ($Pd[P(t\text{-}Bu)_3]_2$, 98%) was obtained from Strem Chemical. Vinyl phosphonic acid (95%) was obtained from TCI Chemicals. Hydrochloric acid (HCl, ACS) was obtained from Macron Fine Chemicals. All glassware was base, acid, and water washed then oven dried. ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR, spectra were obtained on a JEOL ECA 500 liquid-state NMR spectrometer and data obtained was manipulated in MestReNova NMR processor software. Microwave synthesis was preformed on a Biotage Initator+ microwave system. Flash chromatography was preformed on a Biotage Isolara Prime flash chromatography system with Biotage Snap Ultra or Biotage Snap Kp-sil cartridges. High-resolution mass spectrometry (HRMS) was preformed using a JEOL JMS-700T The TandemMStation by a direct probe injection. The samples were ionized by positive electron ionization (EI+) and the spectrum was generated by linear ejection fraction (EF-Linear). All samples were calibrated by an internal standard of Perfluorokerosene-H (PFK, Alfa Aesar Lot #C03T024). The ion peak and the predicted ion peak are located in the Table S1 below.

Phosphonic Acid synthesis

Microwave phosphonic acid synthesis – Under ambient air a 20 mL Biotage microwave vial equipped with a magnetic stir bar was charged with the aromatic halide, vinyl phosphonic acid, N,N-dicyclohexylmethylamine, $Pd[P(t\text{-}Bu)_3]_2$ (catalyst used at 1 mol % level), and THF. The mixture was heated to 180°C at 12 Bar for 15 min, upon completion and cooling workup followed crude PA purification below.

Traditional phosphonic acid synthesis - A Schlenk flask equipped with a magnetic stir bar under argon was charged with the aromatic halide, vinyl phosphonic acid, N,N-dicyclohexylmethylamine, $Pd[P(t\text{-}Bu)_3]_2$ (catalyst used at 1 mol % level), and THF. The mixture was heated to 70°C for 24 h and periodically tested via TLC for reaction completion, upon completion and cooling followed crude PA purification below

Crude phosphonic acid purification - The crude product mixture was extracted three times with ethyl acetate and acidic water (5% HCl). The organic layer was dried with $MgSO_4$, filtered, and the solvent removed using a rotary evaporator. The resultant product was then further purified by recrystallization in ACN or precipitation in DCM.

3 - (E)-(4-(trifluoromethyl)styryl)phosphonic acid -

Synthesis followed microwave PA synthesis procedure above, utilizing 4-(trifluoromethyl) bromobenzene as the aromatic halide. However, as noted in the main text, purification of the reaction crude was first treated in an acidic aqueous (5% HCl/vol) organic EA extraction. Then, the organic fraction was dried with magnesium sulfate, and the solvent was concentrated under rotory evaporation to a volume of only a few milliliters. Finally, **3** was isolated by precipitation into DCM and filtration producing a bright white powder. This compound has been previously synthesized and reported[1, 2] and the ^{1}H NMR (Figure S1) and HRMS (Table S1) characterization matches appropriately.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.80 (s, 2H), 7.71 (s, 2H), 7.26 (dd, 1H), 6.65 (dd, 1H), 5.72 (s, 2H).

4 - (E)-(3,5-difluoro-4-(trifluoromethyl)styryl)phosphonic acid

Synthesis followed the microwave PA synthesis procedure above, utilizing (3,5-difluoro-4-(trifluoromethyl) bromobenzene as the aromatic halide. However, as noted in the main text, purification of the reaction crude was first treated in an acidic aqueous (5% HCl/vol) organic EA extraction. Then, the organic fraction was dried with magnesium sulfate, and the solvent was concentrated under rotory evaporation to a volume of only a few milliliters. Finally, **4** was isolated by precipitation into DCM and filtration producing white flakes. To our knowledge this is a novel compound. See Figures S2-S5 for corresponding NMR spectra and HRMS (Table S1).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.71 (d, J = 11.6 Hz, 2H), 7.14 (dd, J = 21.2 Hz, 1H), 6.84 (dd, J = 17.4, 14.7 Hz, 1H), 5.72 (s, 2H).

^{13}C NMR (126 MHz, DMSO-D_6) δ 167.37, 160.68-158.64 (D J_{C-P} =160Hz 1C), 142.52, 140.36, 125.54 (2C), 123.10-120.93 (d, J_{C-P} 122Hz 1C) 113.27, 113.08, 39.92.

^{19}F NMR (471 MHz, DMSO-D_6) δ -55.20, -112.07.

^{31}P NMR (202 MHz, DMSO-D_6) δ 11.85.

5 - (E)-(2,6-difluorostyryl)phosphonic acid

Synthesis followed the microwave PA synthesis procedure above utilizing 2,6-difluoroiodobenzene as the aromatic halide, However, as noted in the main text, purification of the reaction crude was first treated in an acidic aqueous (5% HCl/vol) organic EA extraction. Then, the organic fraction was dried with magnesium sulfate, and the solvent was concentrated under rotor evaporation to a volume of only a few milliliters. Finally, **5** was isolated by precipitation into DCM and filtration yielding brilliantly white flakes. this compound has been previously synthesized and reported[1, 2], NMR (Figure S6) and HRMS (Table S1) and characterization matches appropriately.

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.06 (s, 1H), 7.43 (t, J = 9.6 Hz, 1H), 7.21 – 7.07 (m, 3H), 6.54 (t, J = 17.5 Hz, 1H).

6 - (E)-(4-methoxystyryl)phosphonic acid

Synthesis followed the microwave PA synthesis procedure above utilizing 4-bromoanisole as the aromatic halide. This compound has been previously synthesized and reported[1, 2] and the ^{1}H NMR characterization matches appropriately (Figure S7).

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 (d, J = 8.7 Hz, 2H), 7.09 (dd, J = 21.9, 17.4 Hz, 1H), 6.91 (d, J = 8.7 Hz, 2H), 6.27 (t, J = 16.9 Hz, 1H), 3.74 (s, 3H).

7 - (E)-(4-(bis(4-methoxyphenyl)amino)styryl)phosphonic acid

Synthesis followed the traditional PA synthesis procedure above utilizing 4-iodo-4',4''-dimethoxytriphenylamine as the aromatic halide, with the exception that once the crude was isolated after extraction, flash chromatography was used to isolate 130mg (31% yield) of a bright yellow highly fluorescent product. To our knowledge this is a novel compound. See Figures S8-S10 for corresponding NMR spectra.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.15 – 6.98 (m, 2H), 6.97 – 6.84 (m, 4H), 6.79 (d, J = 14.0 Hz, 4H), 6.69 (d, J = 27.2 Hz, 2H), 6.27 – 6.07 (m, 1H), 3.71 – 3.63 (m, 6H).

^{13}C NMR (126 MHz, DMSO-D_6) δ 156.04, 155.74, 147.82, 146.94, 141.18, 140.71, 138.55, 133.46, 129.97, 128.89, 128.58, 128.18, 127.72, 127.30, 126.98, 126.76, 126.43, 126.34, 121.31, 120.42, 115.35, 115.28, 55.69, 55.67, 40.05, 21.80.

8 - (*E*)-(3,5-difluorostyryl)phosphonic acid

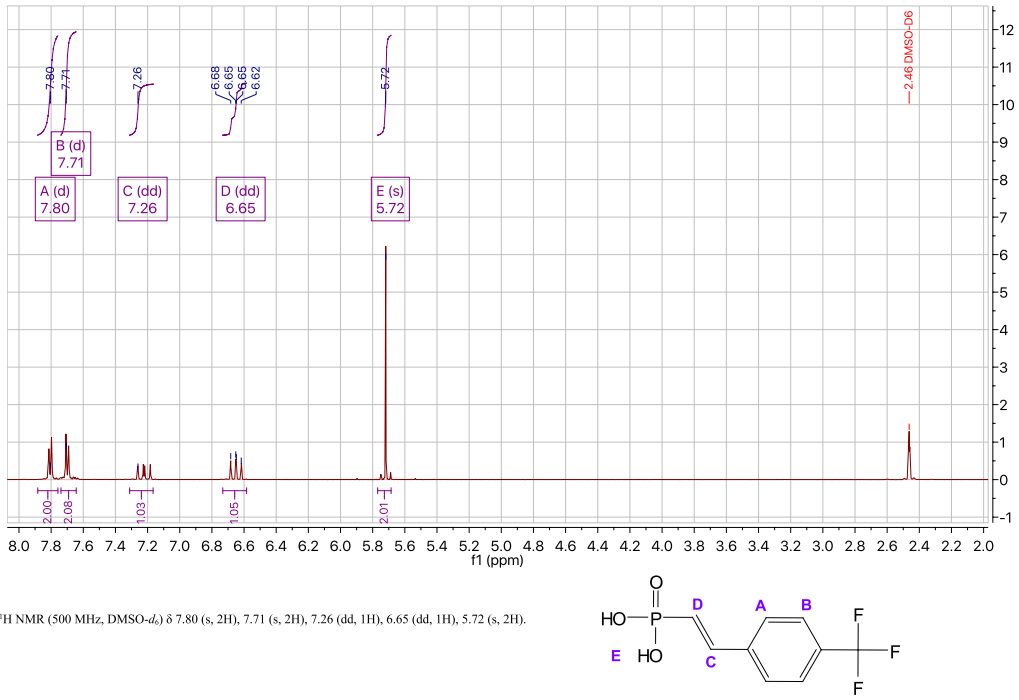
Synthesis followed microwave PA synthesis procedure above utilizing 3,5-difluorobromobenzene as the aromatic halide, this compound has been previously synthesized and reported[1, 2] and the ^{1}H NMR (Figure S11) and HRMS (Table S1) characterization matches appropriately.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.42 – 7.33 (m, 2H), 7.20 – 7.16 (m, 1H), 7.11 (dd, J = 20.2 Hz, 1H), 6.63 (dd, J = 16.5 Hz, 1H).

Table S1 HRMS DATA for select phosphonic acids

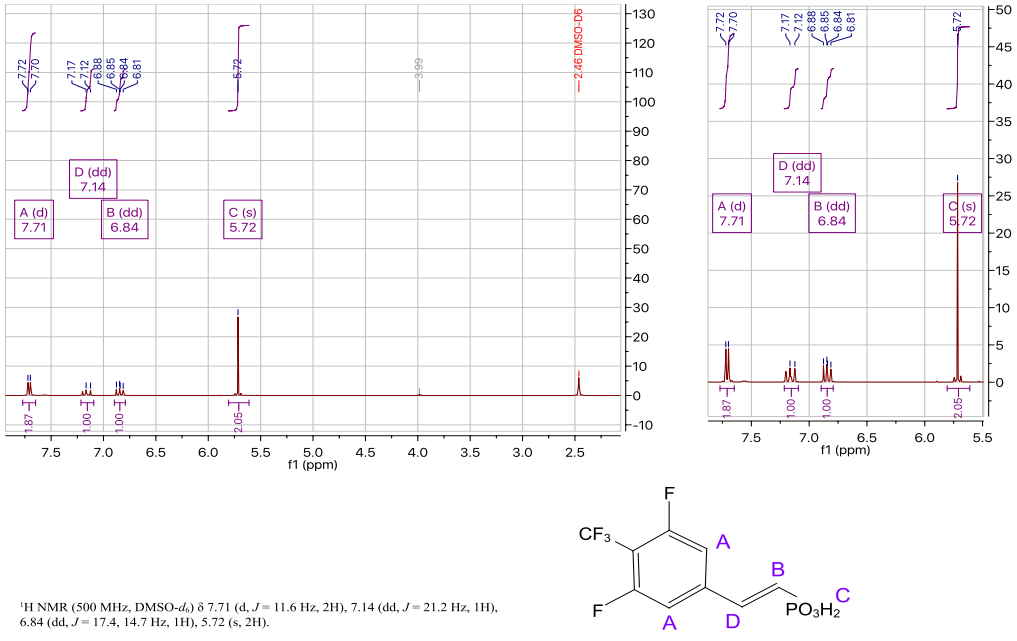
Phosphonic Acid	Observed Ion Peak (m/z)	Predicted Ion Peak (m/z)	Difference (mmu)
3	252.0160	252.0164	-0.4
4	287.9961	287.9974	-1.3
5	220.0097	220.0101	-0.4
8	220.0098	220.0101	-0.3

Selected NMR of Synthesized products



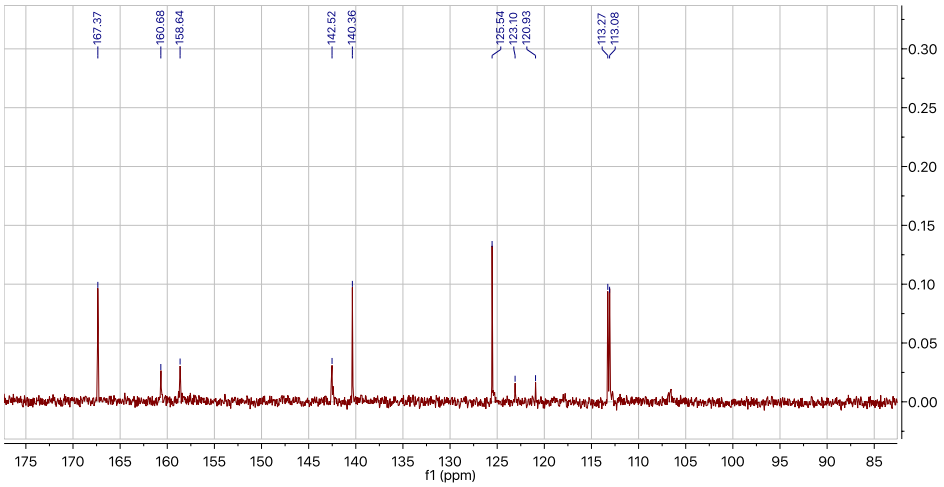
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.80 (s, 2H), 7.71 (s, 2H), 7.26 (dd, 1H), 6.65 (dd, 1H), 5.72 (s, 2H).

Figure S1 - ^{1}H NMR of CF3PA- (E)-(4-(trifluoromethyl)styryl)phosphonic acid (3)



^{1}H NMR (500 MHz, DMSO-d_6) δ 7.71 (d, J = 11.6 Hz, 2H), 7.14 (dd, J = 21.2 Hz, 1H), 6.84 (dd, J = 17.4, 14.7 Hz, 1H), 5.72 (s, 2H).

Figure S2 – ^{1}H NMR of (E)-(3,5-difluoro-4-(trifluoromethyl)styryl)phosphonic acid (4)



^{13}C NMR (126 MHz, DMSO-D_6) δ 167.37, 160.68-158.64 (D $J_{C\text{-}P}$=160Hz 1C), 142.52, 140.36, 125.54 (2C), 123.10-120.93 (d, $J_{C\text{-}P}$ 122Hz 1C) 113.27, 113.08, 39.92.

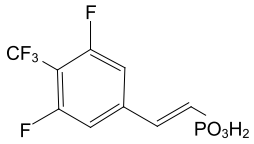
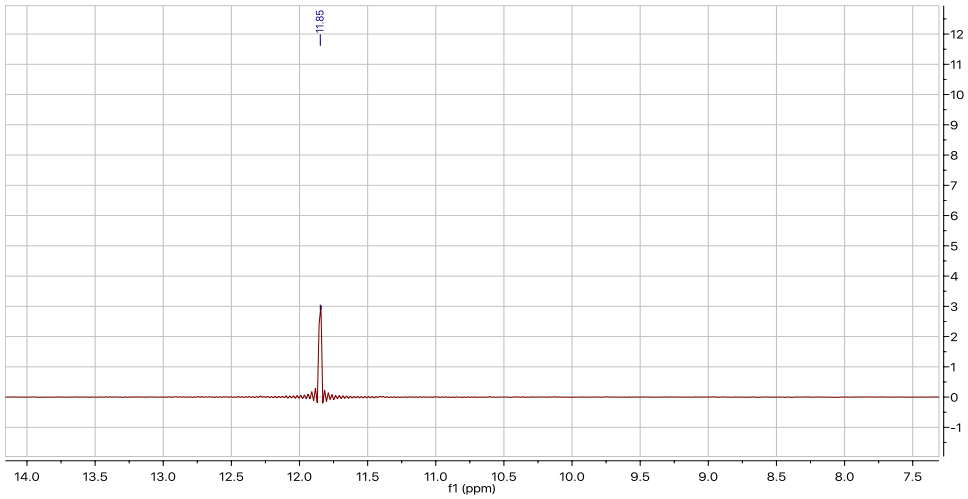


Figure S3 – ^{13}C NMR of (E)-(3,5-difluoro-4-(trifluoromethyl)styryl)phosphonic acid (4)



^{31}P NMR (202 MHz, DMSO-D_6) δ 11.85.

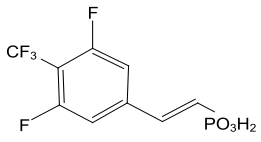
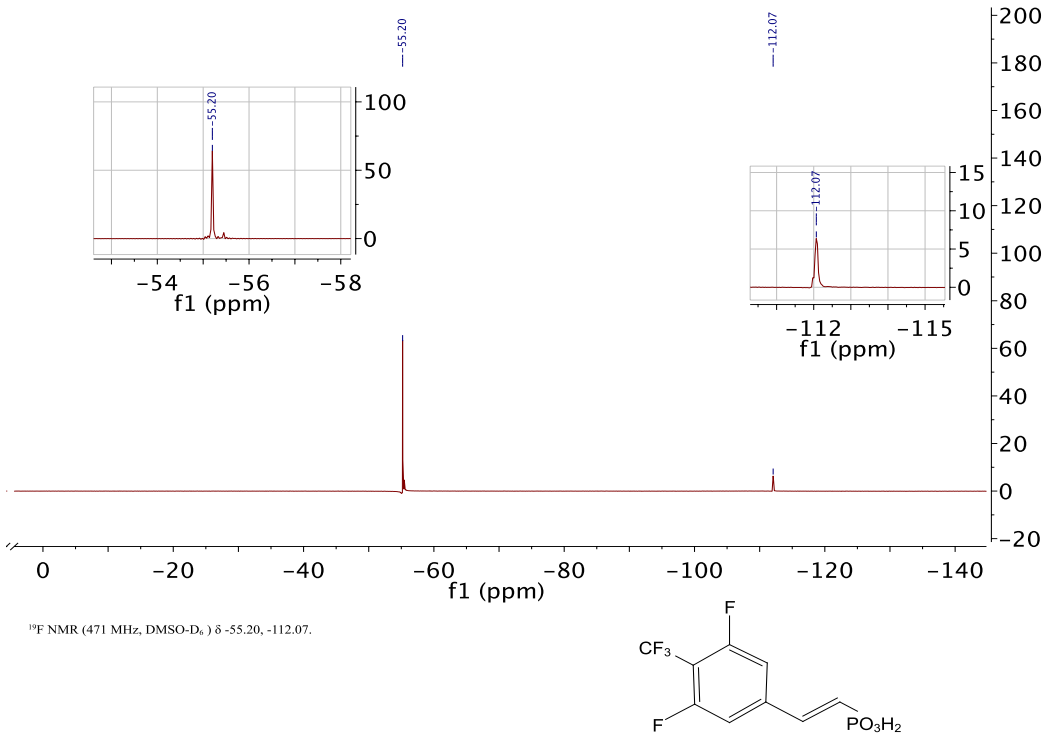
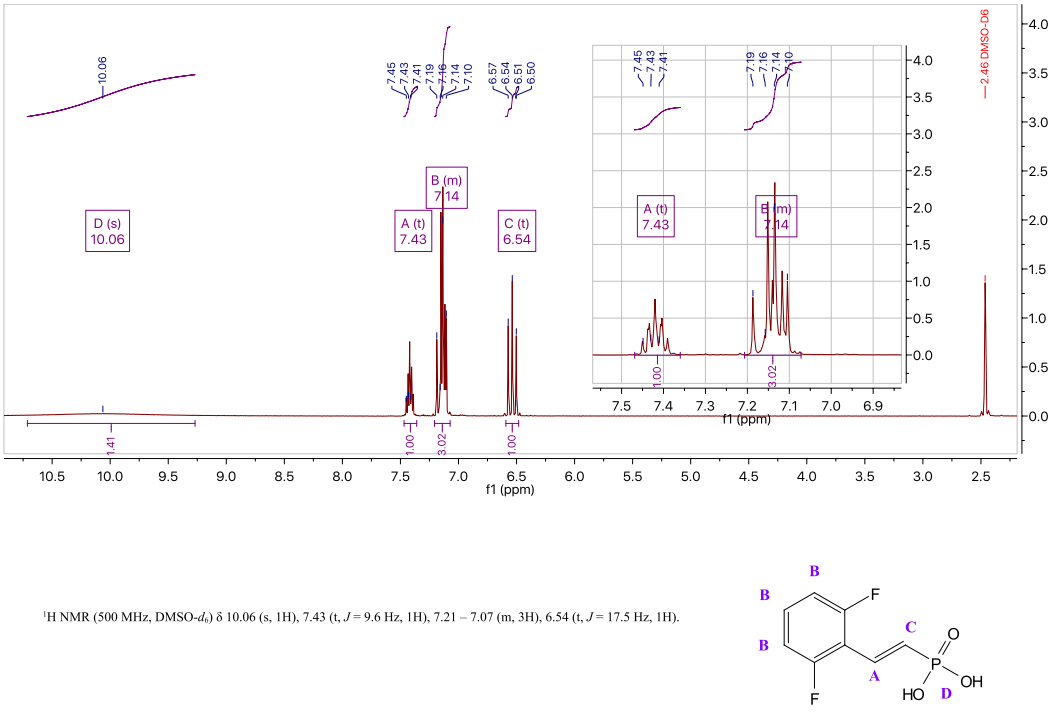


Figure S4 – ^{31}P NMR of (E)-(3,5-difluoro-4-(trifluoromethyl)styryl)phosphonic acid (4)



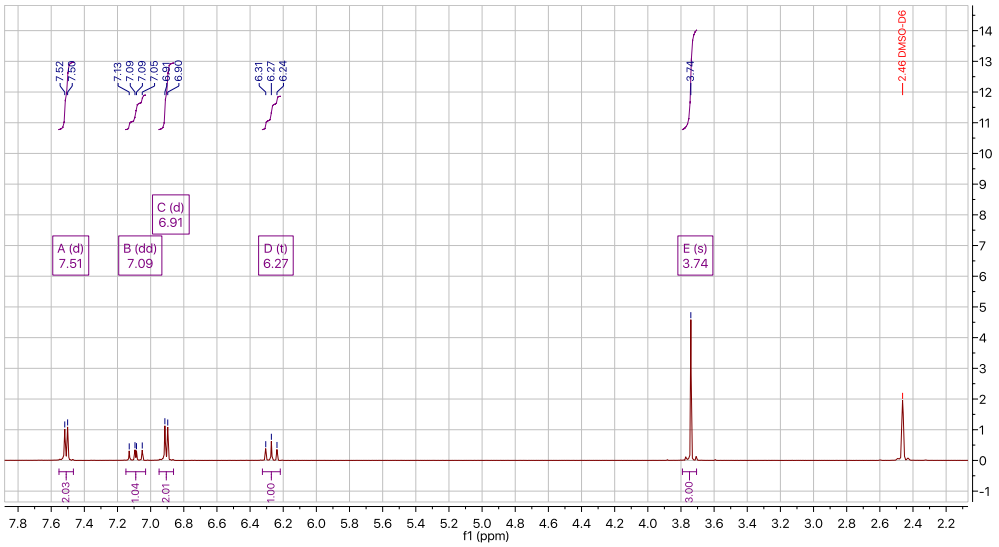
^{19}F NMR (471 MHz, DMSO-D$_6$) δ -55.20, -112.07.

Figure S5 – ^{19}F NMR of (E)-(3,5-difluoro-4-(trifluoromethyl)styryl)phosphonic acid (4)



^{1}H NMR (500 MHz, DMSO-d_6) δ 10.06 (s, 1H), 7.43 (t, J = 9.6 Hz, 1H), 7.21 – 7.07 (m, 3H), 6.54 (t, J = 17.5 Hz, 1H).

Figure S6 – ^{1}H NMR of (E)-(2,6-difluorostyryl)phosphonic acid (5)



^{1}H NMR (500 MHz, DMSO-d_6) δ 7.51 (d, J = 8.7 Hz, 2H), 7.09 (dd, J = 21.9, 17.4 Hz, 1H), 6.91 (d, J = 8.7 Hz, 2H), 6.27 (t, J = 16.9 Hz, 1H), 3.74 (s, 3H).

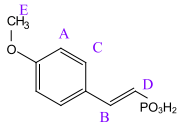
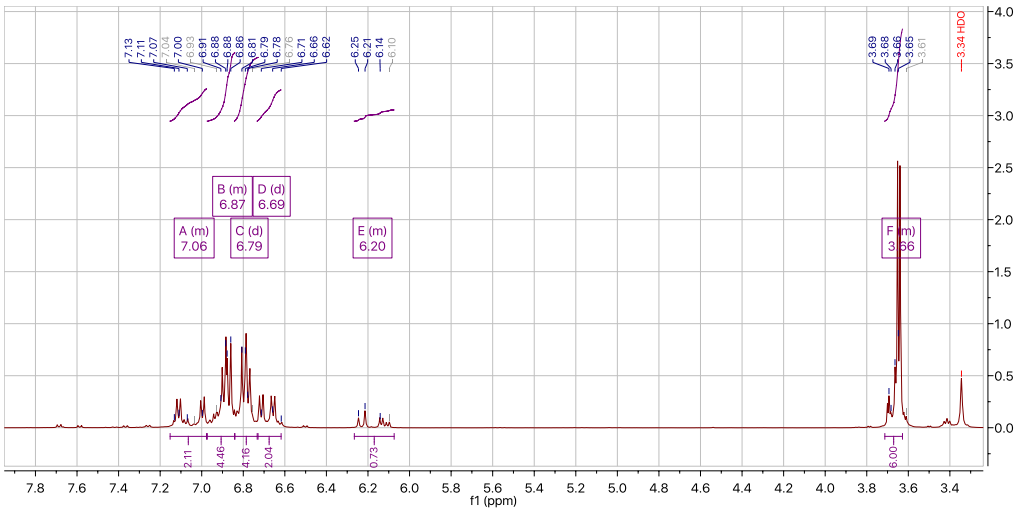


Figure S7 – ^{1}H NMR of (E)-(4-methoxystyryl)phosphonic acid (6)



^{1}H NMR (500 MHz, DMSO-d_6) δ 7.15 – 6.98 (m, 2H), 6.97 – 6.84 (m, 4H), 6.79 (d, J = 14.0 Hz, 4H), 6.69 (d, J = 27.2 Hz, 2H), 6.27 – 6.07 (m, 1H), 3.71 – 3.63 (m, 6H).

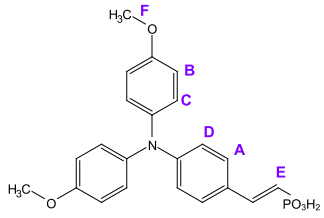


Figure S8 – ^{1}H NMR of (E)-(4-(bis(4-methoxyphenyl)amino)styryl)phosphonic acid (7)

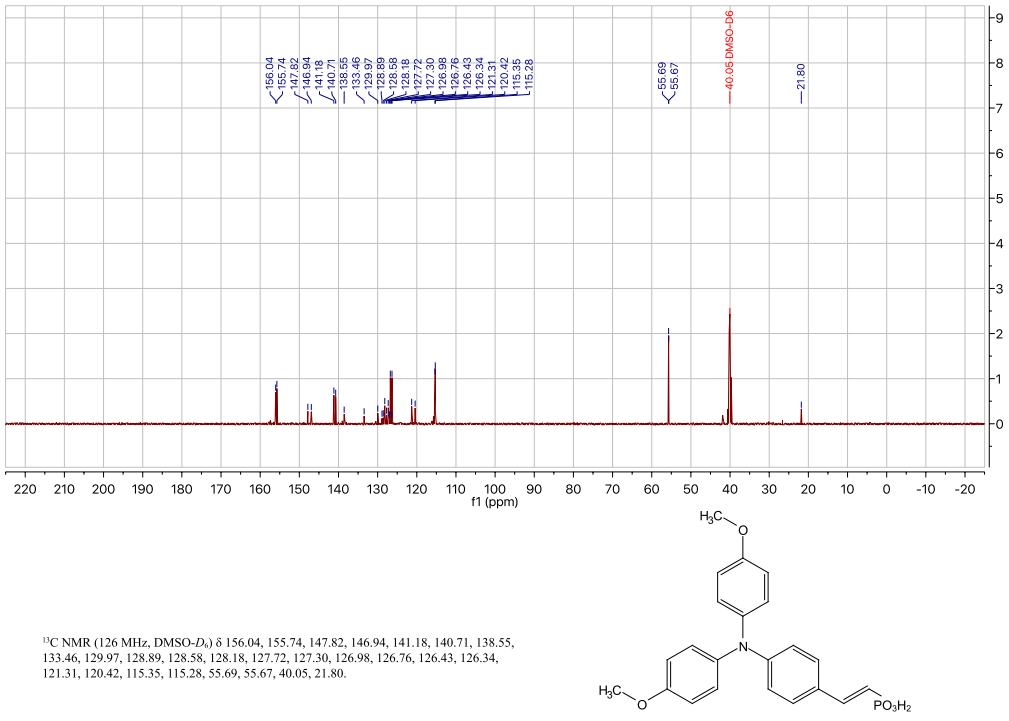


Figure S9 – ^{13}C NMR of (E)-(4-(bis(4-methoxyphenyl)amino)styryl)phosphonic acid (7)

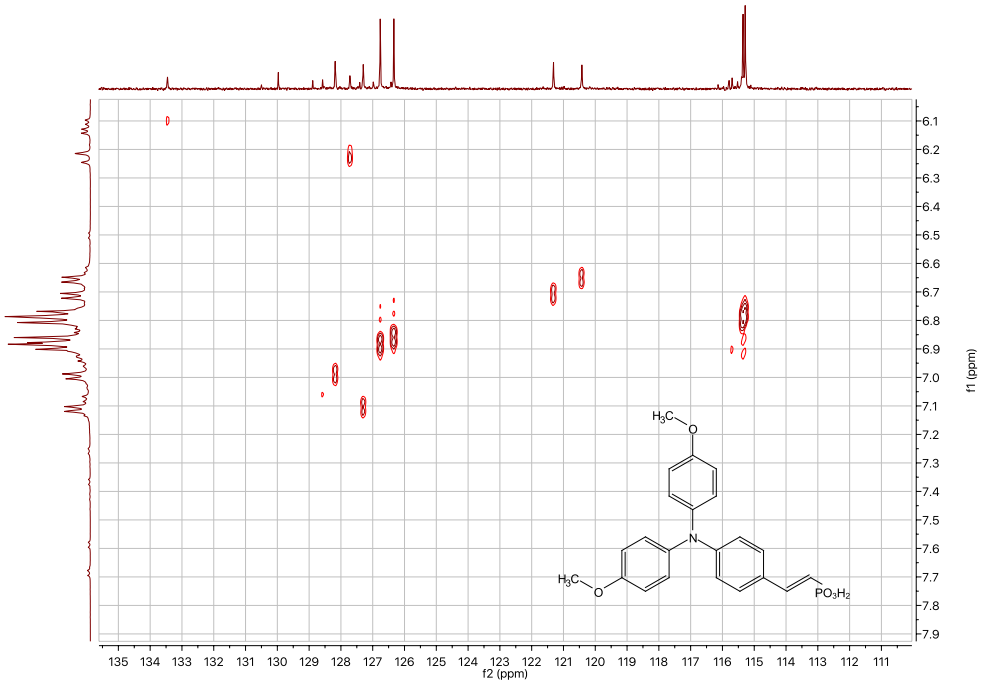


Figure S10 – Two dimensional heteronuclear correlation (HETCOR) of (E)-(4-(bis(4-methoxyphenyl)amino)styryl)phosphonic acid (7)

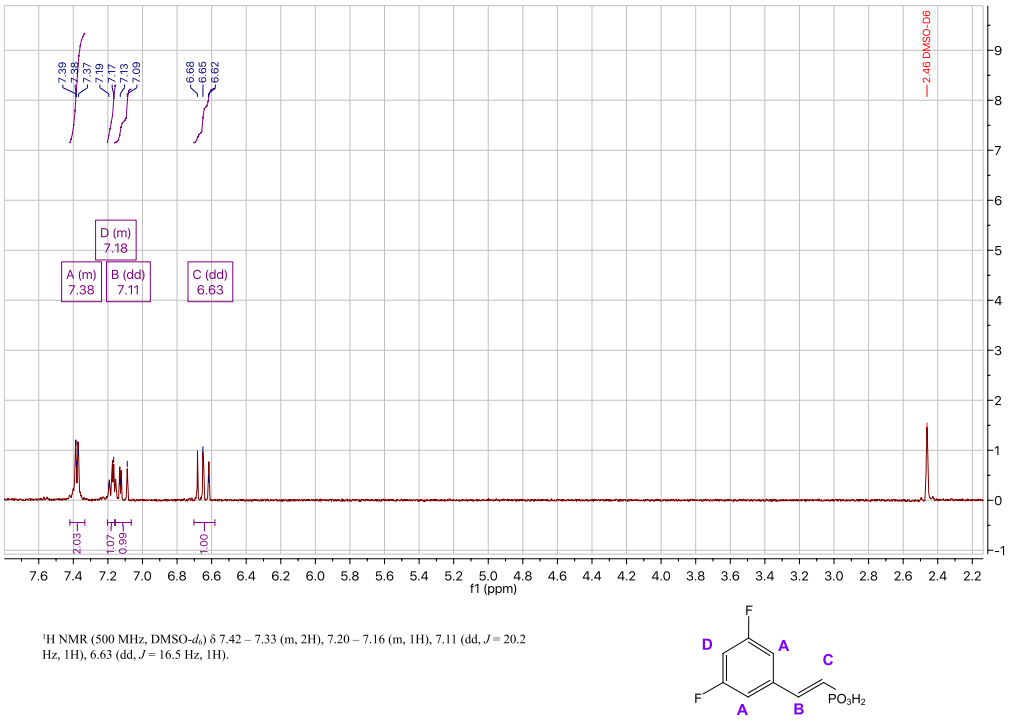


Figure S11 – ^{1}H NMR of (*E*)-(3,5-difluorostyryl)phosphonic acid (8)

References

1. J. L. Braid, U. Koldemir, A. Sellinger, R. T. Collins, T. E. Furtak and D. C. Olson, *ACS Appl. Mater. Interfaces*, 2014, **6**, 19229-19234.
2. U. Koldemir, J. L. Braid, A. Morgenstern, M. Eberhart, R. T. Collins, D. C. Olson and A. Sellinger, *J. Phys. Chem. Lett.*, 2015, **6**, 2269-2276.