Solvent-induced infrared frequency shifts in aromatic nitriles are quantitatively described by the vibrational Stark effect

Nicholas M. Levinson[1], Stephen D. Fried[1], Steven G. Boxer[1*]

[1] Department of Chemistry, Stanford University, Stanford, CA 94305-5080, USA

[*] To whom correspondence should be addressed. E-mail: sboxer@stanford.edu

Supporting Information

Figures

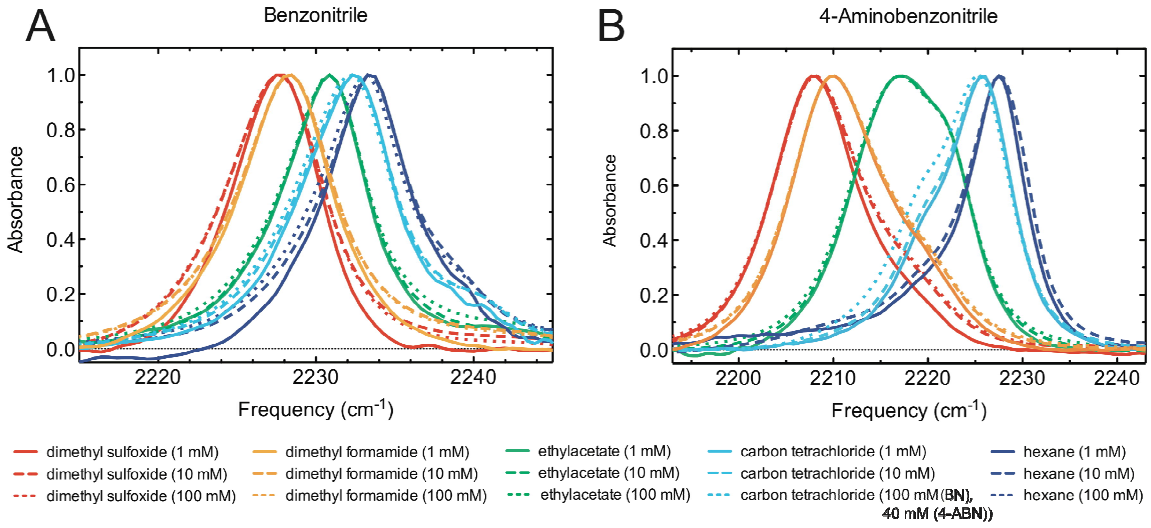

Figure S1. Concentration dependence of the nitrile stretching bands in five different solvents. A) FTIR spectra of benzonitrile are shown for concentrations of 1, 10 and 100 mM, normalized to an absorbance of 1.0. B) FTIR Spectra of 4-Aminobenzonitrile are shown for different concentrations, normalized to an absorbance of 1.0. This compound was not soluble above 10 mM in hexane, and 40 mM in carbon tetrachloride.

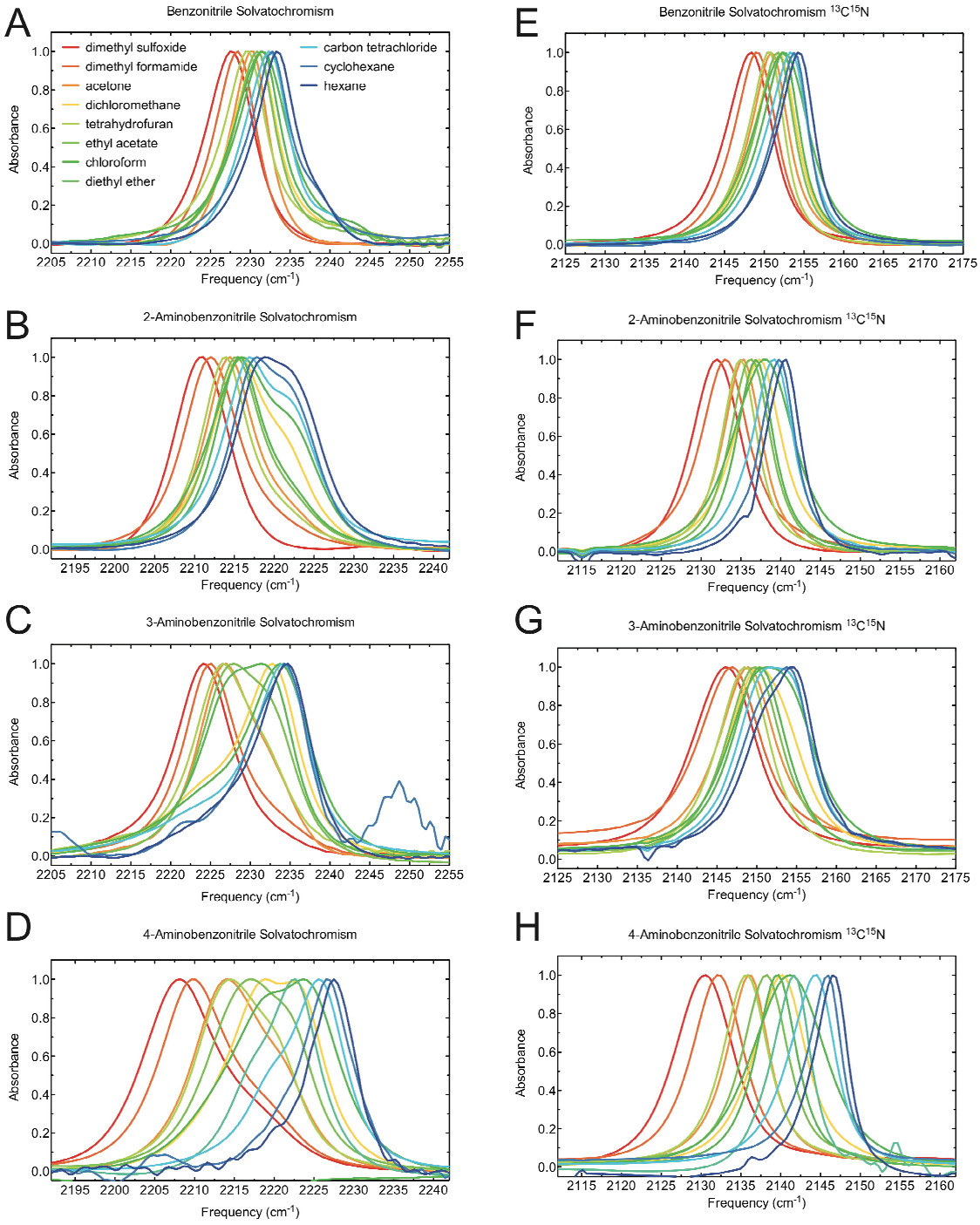

Figure S2. FTIR spectra of the (amino)benzonitriles used in this study dissolved in eleven non-protic solvents. A)-D) FTIR spectra of unlabeled compounds. E)-H) FTIR spectra of isotopically labeled compounds. All compounds were at 10 mM concentration and the spectra are scaled to an absorbance of 1.0.

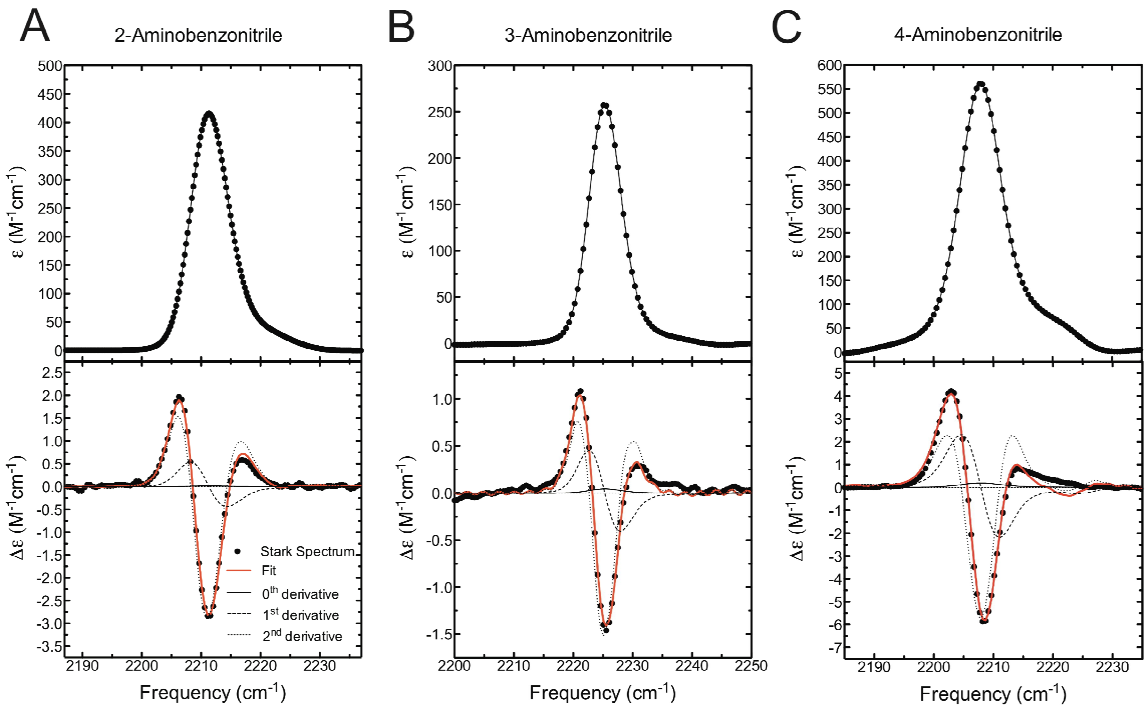

Figure S3. Absorbance (top panels) and Stark spectra (bottom panels) of unlabeled aminobenzonitriles. Samples were at 100 mM concentration in 2-methyltetrahydrofuran at 77K. A) 2-Aminobenzonitrile. B) 3-Aminobenzonitrile. C) 4-Aminobenzonitrile. In the bottom panels, the black dots represent the experimental Stark spectra, the red lines are the numerical fits comprised of a sum of the derivatives of the absorption spectra, and the thin black and dotted lines are the individual contributions of each derivative to the fits. The linear Stark tuning rate is proportional to the square root of the 2nd derivative component of the fit.

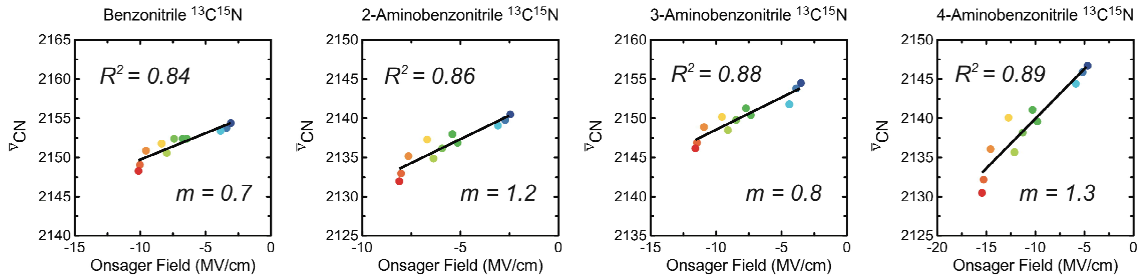

Figure S4. Onsager plots of nitrile stretch frequency versus Onsager reaction field for the isotopically labeled (amino)benzonitriles. The reaction field is the field given by eq 2 in the main manuscript, using the value of 170 Å^3, derived from the molecular volume of benzonitrile, for the parameter a^3 (the Onsager cavity radius cubed). The slopes of the best-fit lines (values of m) represent *apparent* linear Stark tuning rates. The slopes of these plots are 0.7, 1.2, 0.8 and 1.3 cm^{-1}/(MV/cm) for BN, 2-ABN, 3-ABN and 4-ABN respectively, in excellent agreement with the values determined from Stark

spectroscopy. Stark spectroscopy measurements are performed on samples dissolved in frozen glass solvents, which is necessary to avoid reorientation of the solute molecules in the applied field. The observation that the frequency shifts observed in solvents at room temperature are consistent with Stark spectroscopy measurements is a nice demonstration that the measurements in a frozen glass adequately capture the response of the probe to a wide range of fields at room temperature.

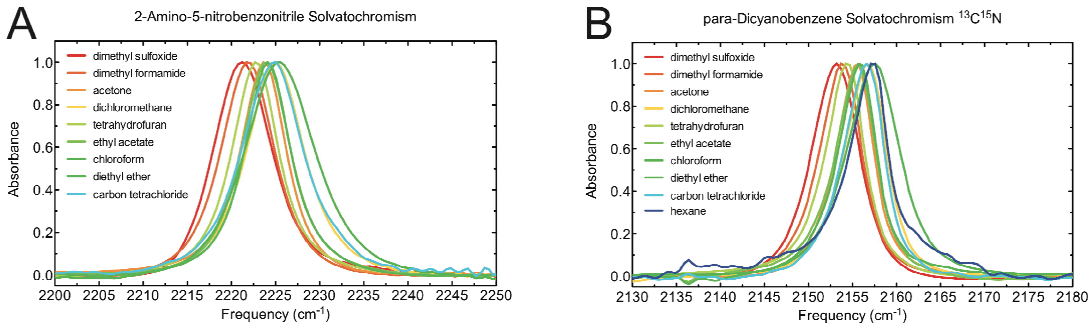

Figure S5. FTIR spectra of 10 mM A) 2-A,5-NBN and B) p-DCB in non-protic solvents. 2-A,5-NBN was not soluble in hexane and cyclohexane, and p-DCB was not soluble in cyclohexane. All spectra were scaled to an absorbance of 1.

Methods

Chemical Synthesis

Copper(I) cyanide. The method from Bagchi and Fried[1] was used in order to prepare $Cu^{13}C^{15}N$. Briefly, copper(II) sulfate was combined with $K^{13}C^{15}N$ (Cambridge Isotopes) in basic aqueous solution and a white powder precipitated, which was collected by filtration.

[$^{13}C^{15}N$]4-aminobenzonitrile. The synthesis was performed as described[1], with the strategy of using an aromatic bromide (rather than an aromatic iodide) to carry out the Rosenmund-von Braun reaction on an aniline coming from literature precedent[2,3]. A conical heavy-walled microwave tube was charged with 4-bromoaniline (Sigma-Aldrich, 46 mg, .29 mmol, 1 equiv), $Cu^{13}C^{15}N$ (50 mg, .58 mmol, 2 equiv), and 0.66 mL anhydrous DMF (Acros Organics). No stir bar was

added; however, vigorous shaking of the microwave tube was employed to completely dissolve the reactants. The solution turned green during dissolution. The microwave tube was sealed with a crimped septum, inserted into a microwave apparatus (Biotage Initiator), and was heated at 170˚C for a 2 h duration at high absorption level. Following irradiation, the black suspension was rinsed with diethyl ether (10 mL) and basic water (.01 M KOH, pH 12, 10 mL) into a separatory funnel. The basic aqueous phase was extracted with diethyl ether (2 × 10 mL), and then the combined organic phase was washed with basic water (2 × 10 mL). The washed organic phase was dried over magnesium sulfate and reduced by rotary evaporation to furnish a yellow residue. ^{1}H NMR of the crude product provided an estimate for the conversion at ca. 72%. The residue was redissolved in 1.5 mL EtOH and was loaded onto an HPLC (Shimadzu LC-20AT prominence) C18 column (A = 0.1% (vol/vol) TFA in ddH_2O; B = acetonitrile) running at 5 mL/min under a gradient where the fraction B linearly steps up from 15% to 60% at a rate of 1 %/min over 45 min. The chromatogram of the crude product contained two major bands (19 – 22 mL, 22 – 27 mL). The latter fraction (22 – 27 mL) – determined to correspond to product because it absorbs light appreciably of 254 nm – was collected and lyophilized overnight (VirTis Freezemobile 12EL) to afford a colorless powder of the title compound (5 mg, 16% yield). ^{1}H NMR(DMSO-d_6 @ 300 MHz): δ 7.38 (ddd[a], J = {2 Hz, 5 Hz, 8.5 Hz}, 2 H), 6.59 (*d*, J = 9 Hz, 2 H), 6.14 (s, 2 H). LCMS: m/z calc'd for [$^{13/15}$**M**] $C_6{}^{13}C_1H_6{}^{15}N_1N_1$ is 120.05. Found: (+) 121.0041 [$^{13/15}$**M**+1].

[a]The splitting pattern arises from coupling to the ^{13}C and the ^{15}N nucleus, which are both spin-½

[^{13}C^{15}N]3-aminobenzonitrile. A method similar to the above was employed. 3-bromoaniline (Sigma-Aldrich, 60 mg, 0.35 mmol, 1 equiv), Cu^{13}C^{15}N (64 mg, 0.70 mmol, 2 equiv), and 1.0 mL anhydrous DMF (Acros Organics) were combined, and heated in a microwave at 170˚C for 2 h. The resulting black suspension was rinsed with diethyl ether and basic water into a separatory funnel. The basic aqueous phase was extracted, and the combined organic phase was washed with basic water.

The washed organic phase was dried over magnesium sulfate and reduced by rotary evaporation to furnish a yellow residue. ^{1}H NMR of the crude product provided a rough estimate for the conversion at ca. 70%, though the spectrum was difficult to interpret. The residue was dissolved in EtOAc, and loaded onto a silica gel column, running 3:7 EtOAc : hexanes. The product was cleanly separated and eluted after the starting material, according to TLC conducted on the individual fractions. The fractions containing only product were combined and reduced by rotary evaporation, to afford a light-brown powder (17 mg, 41% yield). ^{1}H NMR($CDCl_3$ @ 300 MHz): δ 7.23 (t, *J* = 8 Hz, 1 H), 7.04-7.00 (m, 1 H), 6.91-6.86 (m, 2 H), 3.88 (s, 2 H). LCMS: m/z calc'd for [$^{13/15}$**M**] $C_6{}^{13}C_1H_6{}^{15}N_1N_1$ is 120.05. Found: (+) 121.0042 [$^{13/15}$**M**+1].

[^{13}C^{15}N]2-aminobenzonitrile. A method similar to the above was employed. 2-bromoaniline (Sigma-Aldrich, 60 mg, 0.35 mmol, 1 equiv), Cu^{13}C^{15}N (64 mg, 0.70 mmol, 2 equiv), and 1.0 mL anhydrous DMF (Acros Organics) were combined, and heated in a microwave at 170˚C for 2 h. The resulting black suspension was rinsed with diethyl ether and basic water into a separatory funnel. The basic aqueous phase was extracted, and the combined organic phase was washed with basic water. The washed organic phase was dried over magnesium sulfate and reduced by rotary evaporation to furnish a yellow residue. ^{1}H NMR of the crude product suggested the conversion was near quantitative. The residue was dissolved in dichloromethane, and loaded onto a silica gel column, running 5% methanol in dichloromethane. The fractions containing only product according to TLC were combined and reduced into a yellow oil by rotary evaporation, which crystallized into yellow needles upon resting in a vial overnight (12 mg, 29% yield). ^{1}H NMR($CDCl_3$ @ 300 MHz): d 7.42-7.30 (m, 2 H), 6.77-6.72 (m, 2 H), 4.38 (s, 2 H). LCMS: m/z calc'd for [$^{13/15}$**M**] $C_6{}^{13}C_1H_6{}^{15}N_1N_1$ is 120.05. Found: (+) 120.940 [$^{13/15}$**M**+1].

[(^{13}C^{15}N)$_1$]p-dicyanobenzene. A conical heavy-walled microwave tube was charged with 4-iodobenzonitrile (Sigma-Aldrich, 69 mg, .30 mmol, 1 equiv),

$Cu^{13}C^{15}N$ (56 mg, .60 mmol, 2 equiv), and 0.5 mL anhydrous DMF (Acros Organics). No stir bar was added; however, vigorous shaking of the microwave tube was employed to completely dissolve the reactants. The solution turned green during dissolution. The microwave tube was sealed with a crimped septum, and inserted into a microwave apparatus (Biotage Initiator), and heated or 150 ˚C for a 1.5 h duration at high absorption level. Following irradiation, the contents of the tube were rinsed with diethyl ether (10 mL) and water (10 mL) into a sep funnel, and insoluble material adhered to the microwave tube was left behind. The aqueous phase was extracted with diethyl ether (2 × 10 mL), and then the combined organic phase was washed with water (2 × 15 mL). The washed organic phase was dried over magnesium sulfate and reduced by rotary evaporation to furnish an off-white powder. ^{1}H NMR of the crude product provided an estimate for the conversation at ca. 86%. The title compound was purified by dissolving the crude product in a minimal volume of boiling EtOH (4 mL), which was allowed to stand on the bench-top overnight to return slowly to room temperature. Colorless crystals appeared, which were collected by filtration over a fine frit, and then washed with cold ethanol (2 × 5 mL). The pure product (11 mg) was obtained in 26% overall yield. ^{1}H NMR($CDCl_3$): δ 7.79 (d, J < 1.5 Hz, 4 H)). ^{13}C NMR($CDCl_3$)[b]: δ 117.13 (d, J = 9 Hz).

[b]A short scan reveals only a single signal to demonstrate the isotopically enriched ^{13}C in the installed nitrile. The doublet corresponds to the scalar coupling of ^{13}C to ^{15}N.

References.

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(2) Akanuma, K.; Amamiya, H.; Hayashi, T.; Watanabe, K.; Hata, K. *Nippon Kagaku Zaeshi* **1962**, *81*, 333.

(3) Ellis, G. P.; Romney-Alexander, T. M. *Chemical Reviews* **1987**, *87*, 779.