Supporting Online Information for:

ANHYDROUS MONOALKYL GUANIDINES IN APROTIC AND NONPOLAR SOLVENTS: MODELS FOR DEPROTONATED ARGININE SIDE CHAINS IN MEMBRANE ENVIRONMENTS

MEMBRANE ENVIRONMENTS

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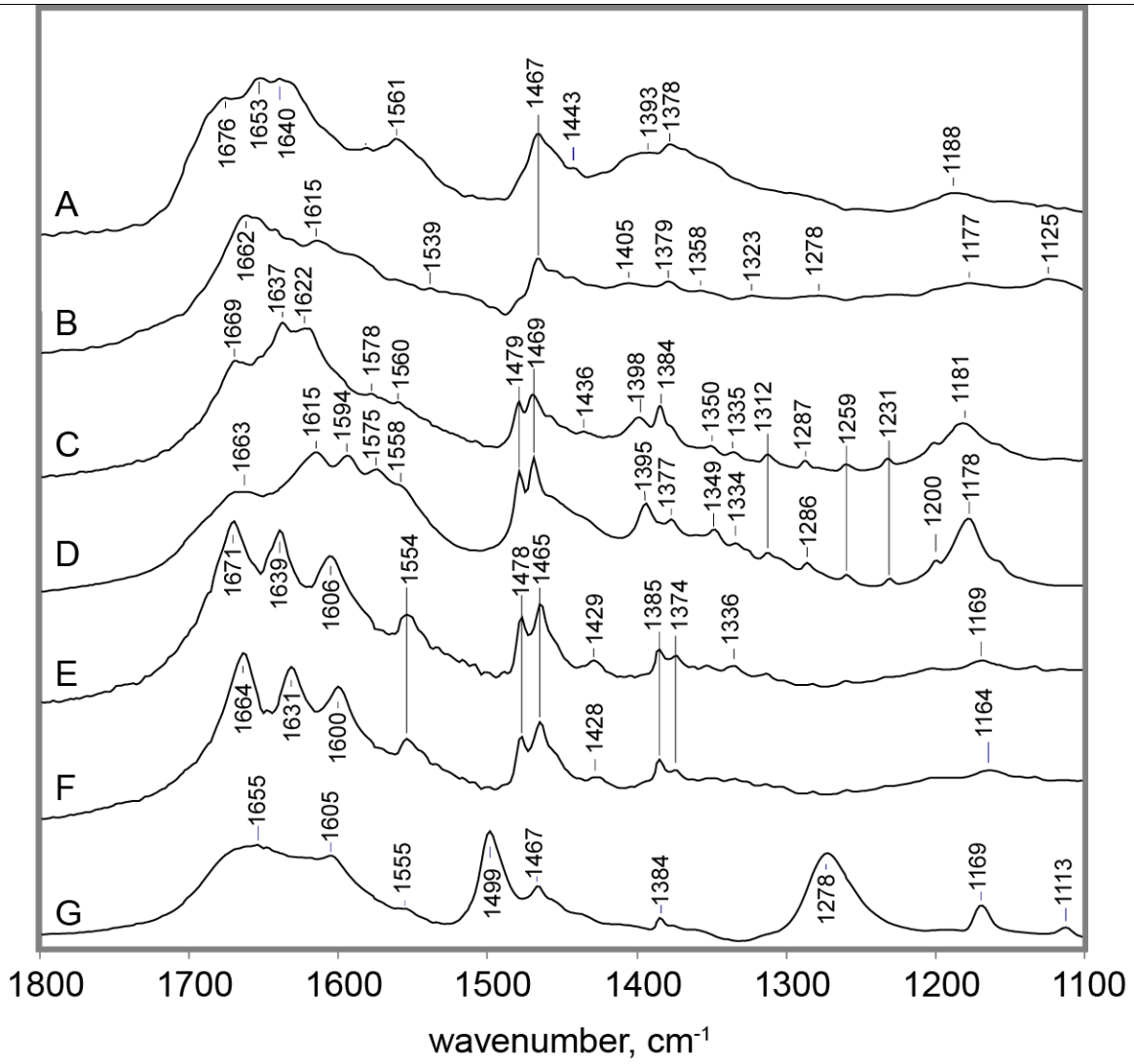
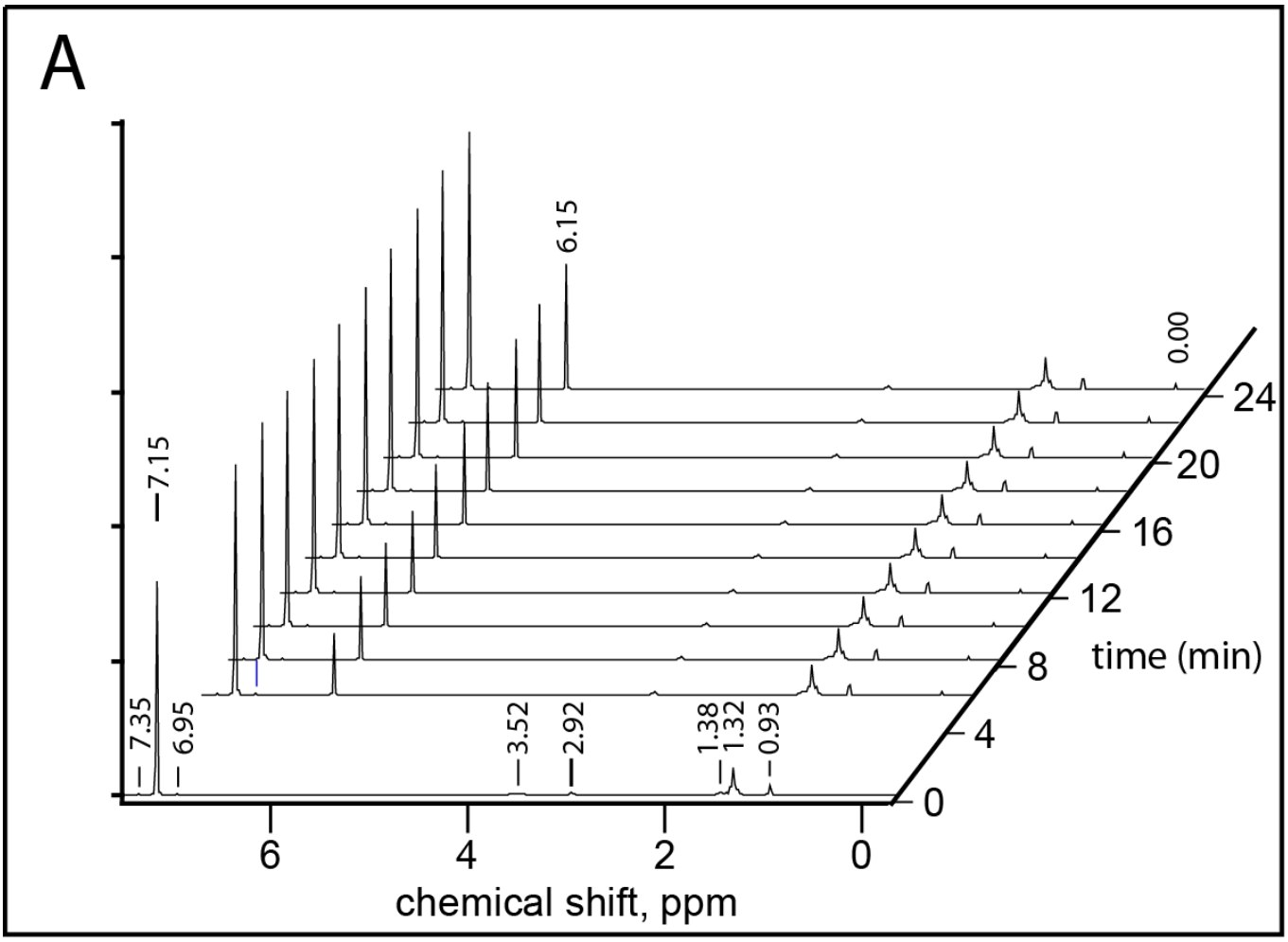
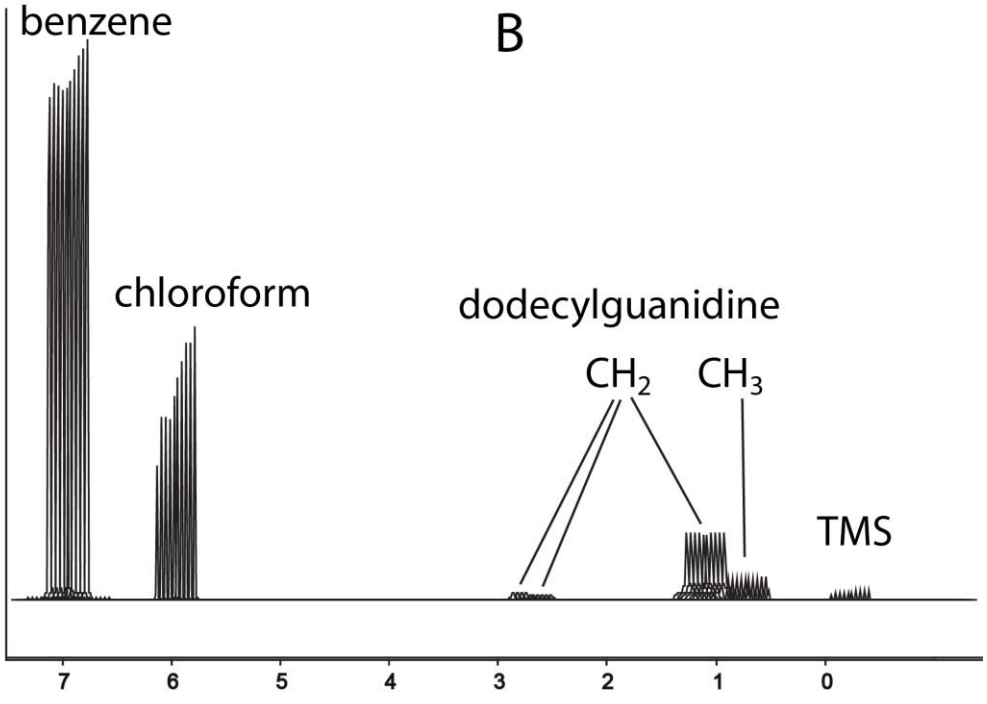


Figure S-1: IR spectra of (**A**) dodecylguanidine free base (**2**), dissolved to saturation in CCl_4; (**B**) dodecylguanidine-$^{15}N_2$ free base (**2´**), also in CCl_4; (**C-G**), measurements of crystalline samples in KBr pellets. (**C**) and (**D**), same dodecyguanidine free-base compounds as (**A**) and (**B**), respectively; (**E**) and (**F**), dodecylguanidinium bromide, in natural isotope abundance and with ^{15}N label (**1**, **1´** respectively); (**G**) phenol-dodecylguanidine (**15**). Spectral quality in **A** and **B** was limited by the low solubility of **2** in CCl_4.


A
6.15
0.00
7.15
24
20
16
12
8
4
0
time (min)
7.35
6.95
3.52
2.92
1.38
1.32
0.93
6
4
2
0
chemical shift, ppm


benzene
B
chloroform
dodecylguanidine
CH2
CH3
TMS
7
6
5
4
3
2
1
0

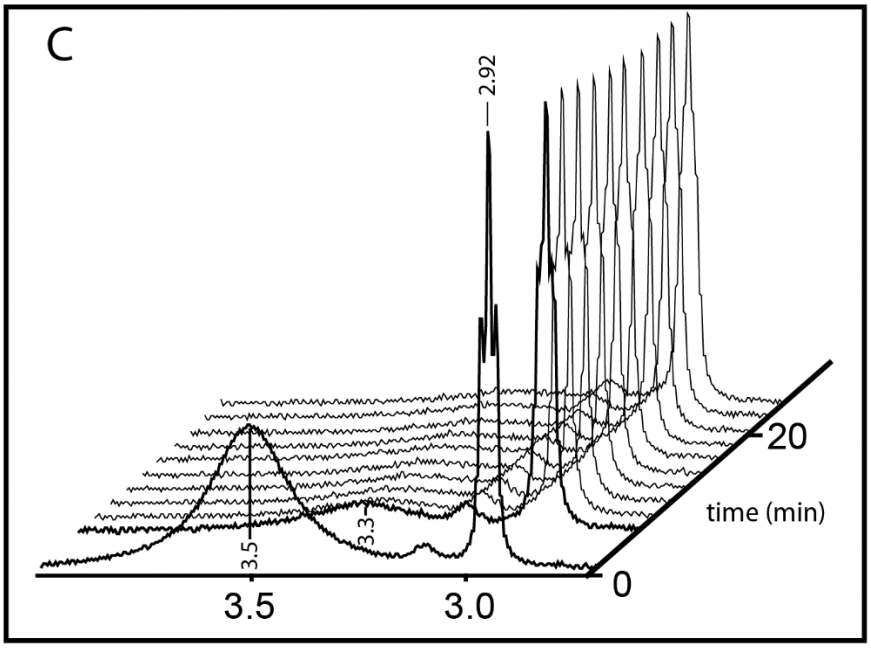


Figure S-2: Time dependent ^{1}H NMR spectra of 0.01 *M* dodecylguanidine free base, allowing the $^{1}H/^{2}H$ exchange process with chloroform-*d* to be followed. These are the raw spectral data that are the basis for Fig. 3 of the main paper. **A** and **B**, full spectral region, with differing relative vertical and horizontal offsets to permit different types of comparisons. **C**, expansion of the region from 2.7-4.0 ppm. The first time point (*t*= 0) was taken in pure benzene-d_6 Subsequent spectra were taken at 2-min intervals beginning at 5 min after addition of 0.50 *M* chloroform-*d*. The *t*=0 spectrum (omitted from **B**) was rescaled vertically to give the same integrated peak size at 2.92 ppm as the later 10 spectra; these 10 were not rescaled relative to each other, so panel B accurately represents the time course of the raw measured intensities. The broad peak at 3.5 ppm at *t*=0 is due to the 4 rapidly-exchanging protons on the deprotonated guanidine group. Its integrated area is ~2 times that of the peak due to the α–methylene protons at 2.92 ppm. Immediately after adding chloroform-*d* to 0.5 *M* (~4%), this peak downshifts to 3.3 ppm and broadens. Other peaks show smaller solvent shifts (unlabeled). The rapid loss of intensity at 3.3 ppm, and the rise at 6.15 ppm, are due to $CHCl_3$ being formed by $^{1}H/^{2}H$ exchange with dodecylguanidine, presumably catalyzed by the latter acting as a very strong base. The final concentration of the protonated chloroform approaches only 0.04 *M*, i.e. 8% of the total $CHCl_3$. This is due to the limited supply of protons from the lower-concentration solute. Other peaks in these spectra include the triplet at 7.15 ppm due to residual protons on benzene-d_6, and its satellite bands at 7.35/6.95 due to coupling with neighboring ^{13}C present at about 1%; multiple peaks from 0.94-1.4 ppm due to the dodecyl chain; and a feature at 0.0 ppm due to tetramethylsilane present in the commercially-supplied chloroform-*d*. These spectra also provide evidence for H/D exchange of the dodecylguanidine free base with benzene-d_6, albeit at a slower rate than for chloroform-*d*. The proton signal at 7.15 ppm at *t*=0 is already a bit larger than obtained for pure benzene-d_6 direct from the commercially-supplied bottle, and during the time interval *t*=5-23 min, its integrated area also increased in size by 11%. When normalized to the size of the signal at 2.92 (considered as 2.0 protons), the increase at 7.15 ppm corresponds to an added 0.4 protons on benzene.

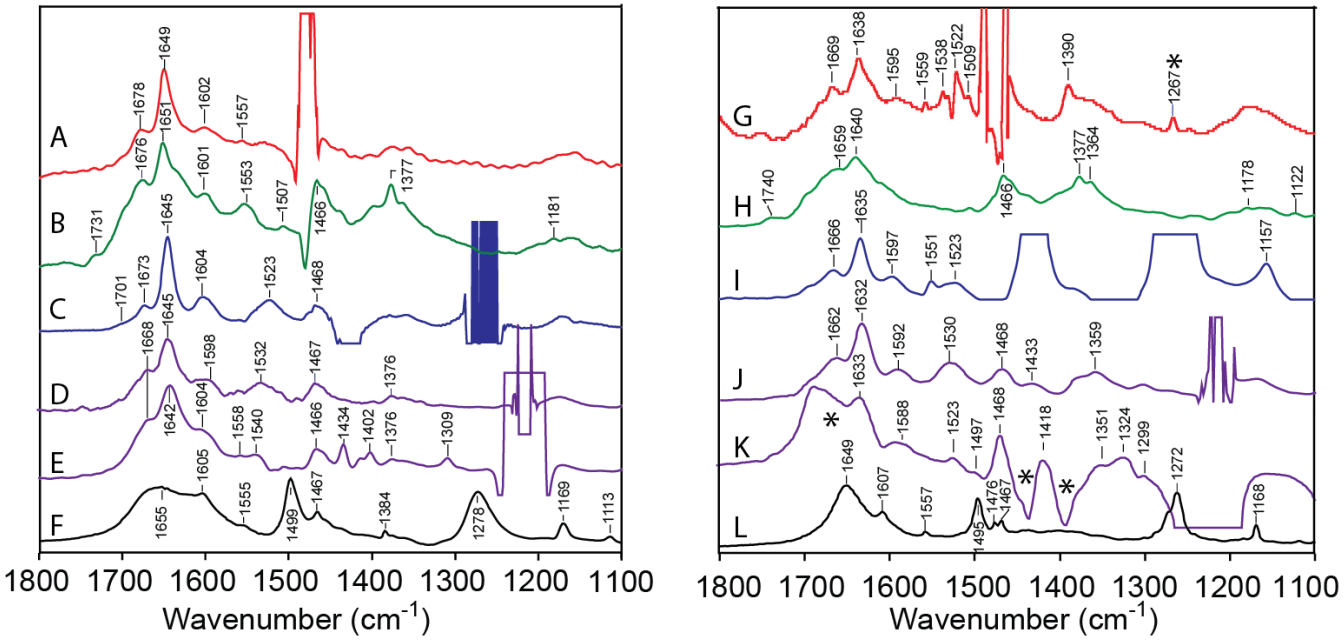


Figure S-3: Left panel (**A-E)**, more extended spectral ranges of the IR spectra of dodecylguanidine free base (**2´**) shown in Figure 1 of the main paper, in the same order as there. Right panel (**G-K**), corresponding measurements with the 2 terminal nitrogens ^{15}N labeled (**2´).** Most spectra were measured in dry nonpolar solvents: benzene (**A, G**); CCl_4 (**B, H**); CH_2Cl_2 (**C, I**); $CHCl_3$ (**D, J**);. Additional solution spectra were measured in water-saturated $CHCl_3$ (**E, K**). A final pair of spectra, provided for comparison, represents crystalline (*p*-phenolyl)-dodecyl-guanidine free base (**15**, **15´**) measured as a KBr pellet either with natural isotope abundance (**F**) or with terminal nitrogens ^{15}N labeled (**L**). Vertical scales were adjusted to facilitate comparisons. Truncated (off-scale) spectral traces are due to noise in specific narrow spectral bands, resulting from strong solvent background absorptions that blocked IR measurements. The untruncated spectra, with accurate individual vertical scales, are available in Figures **S-3** to **S-12** below. The asterisk (*) at 1267 cm-1 in spectrum **G** indicates this is due to a contaminant that formed slowly over time (see Figure S-9 below for details). Asterisks in spectrum **K** indicate that the bandshapes near 1650, 1425, and 1390 cm^{-1} are particularly unreliable, due to difficulties in subtracting solvent absorbance in these regions. These problems were worse for spectra **G** and **K** than **A** and **E**, respectively, due to the lower concentration of isotope-labeled solute that was available.

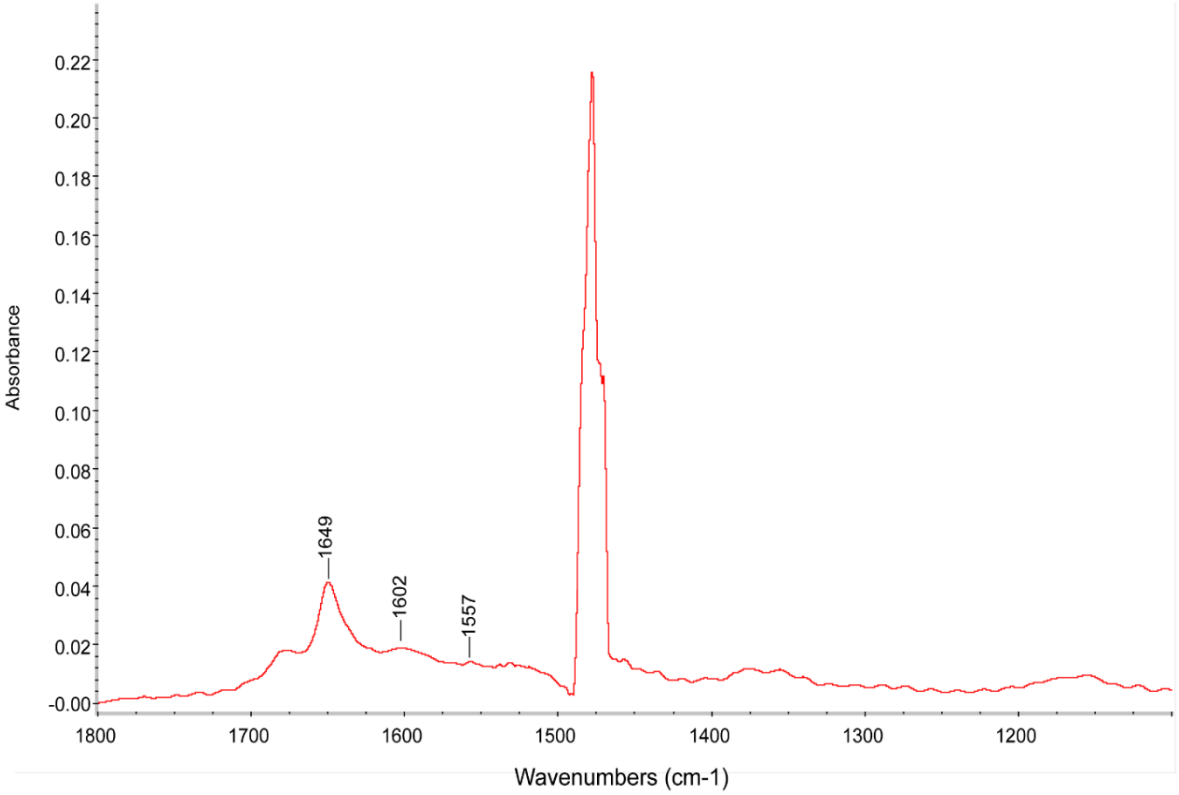


Figure S-4. IR absorbance spectrum of Figure **S-3A**, shrunk to fit on-scale. Dodecylguanidine free base (compound **2**), in benzene, vs. the same solvent, with additional subtraction of the absorbance spectrum of the neat solvent, in order to produce the flattest possible baseline.

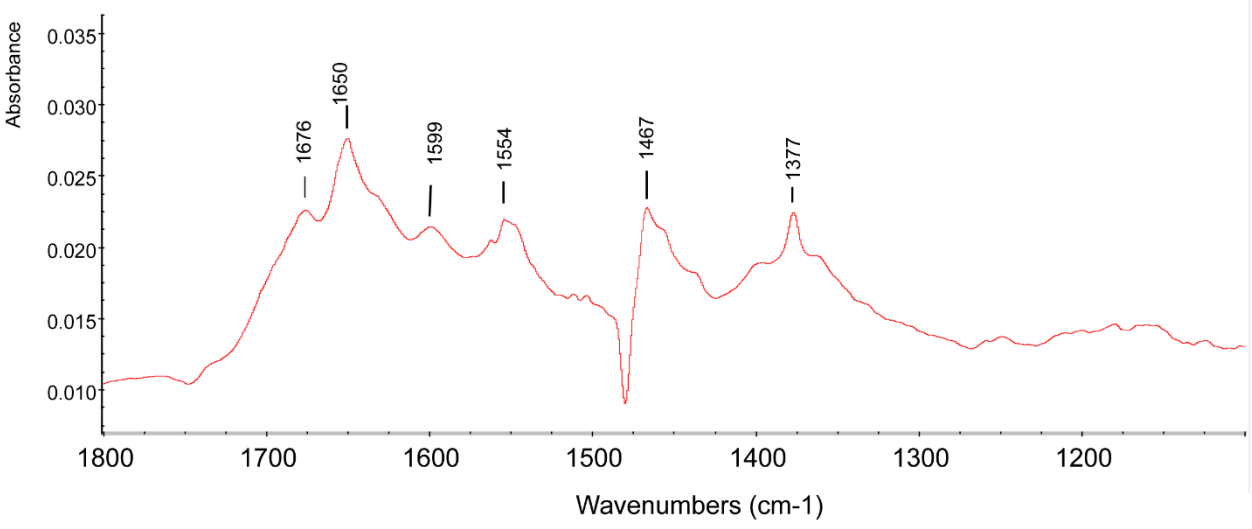


Figure S-5. IR absorbance spectrum of Figure **S-3B**, shrunk to fit on-scale. Dodecylguanidine free base (compound **2**), in CCl_4, vs. the same solvent; with additional subtraction of the absorbance spectrum of the neat solvent, in order to produce the flattest possible baseline.

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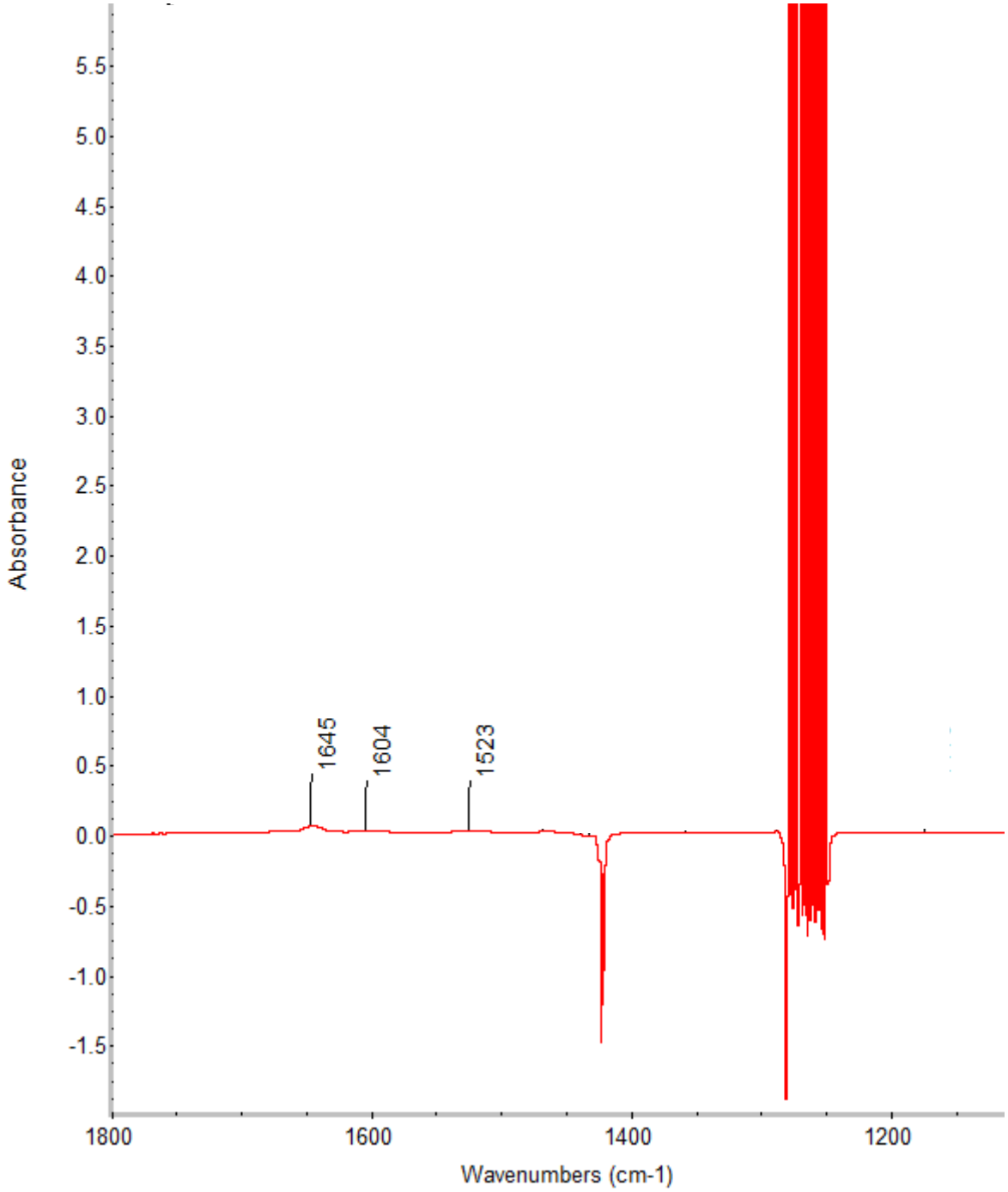

Figure S-6. IR absorbance spectrum of Figure **S-3C**, shrunk to fit on-scale. Dodecylguanidine free base (compound **2**), in CH_2Cl_2, vs. the same solvent; with additional subtraction of the absorbance spectrum of the neat solvent, in order to produce the flattest possible baseline.

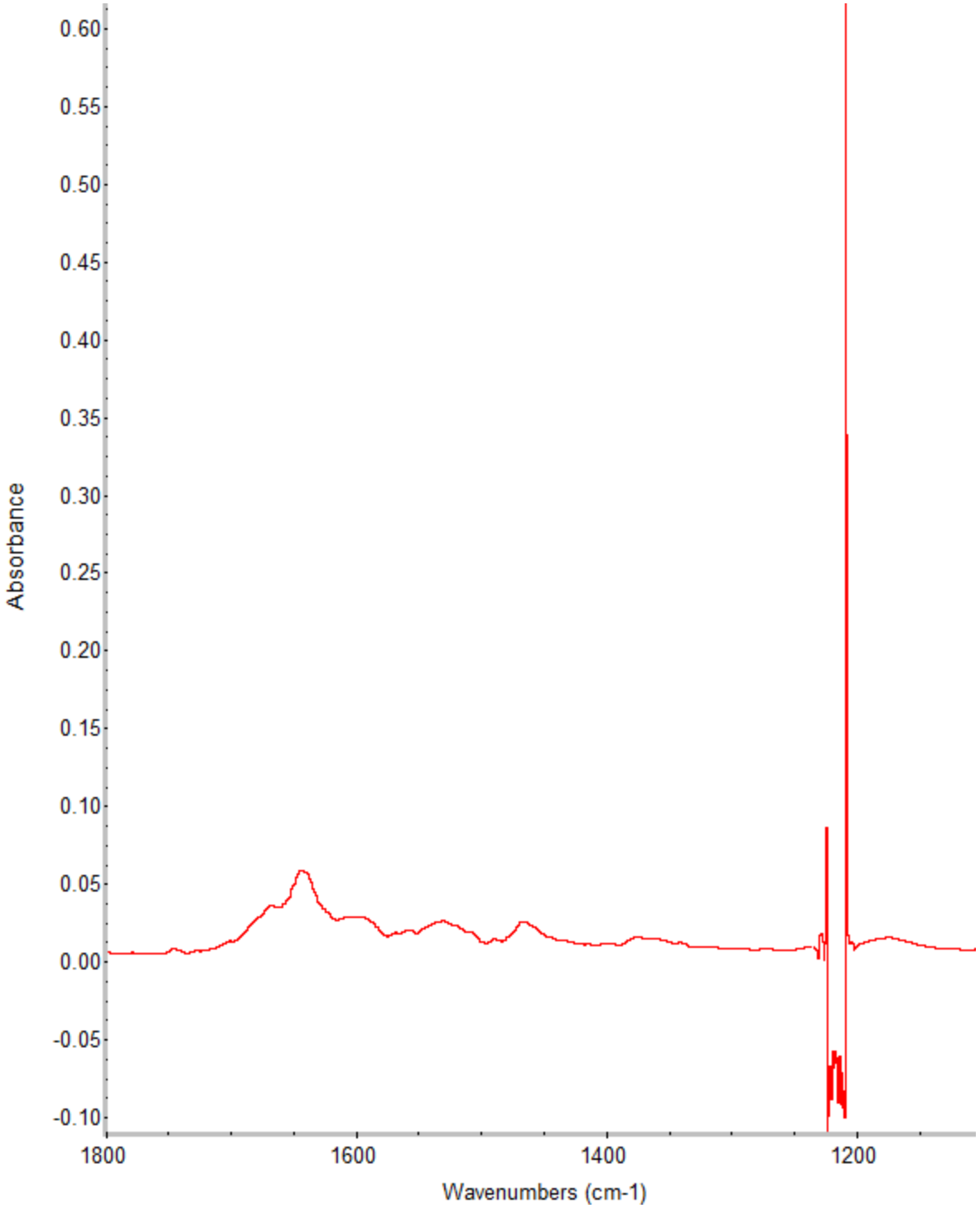

Figure S-7. IR absorbance spectrum of Figure **S-3D**, shrunk to fit on-scale. Dodecylguanidine free base (compound **2**), in chloroform ($CHCl_3$), vs. the same solvent. Additional subtraction of the absorbance spectrum of the neat solvent was then performed, in order to produce the flattest possible baseline.

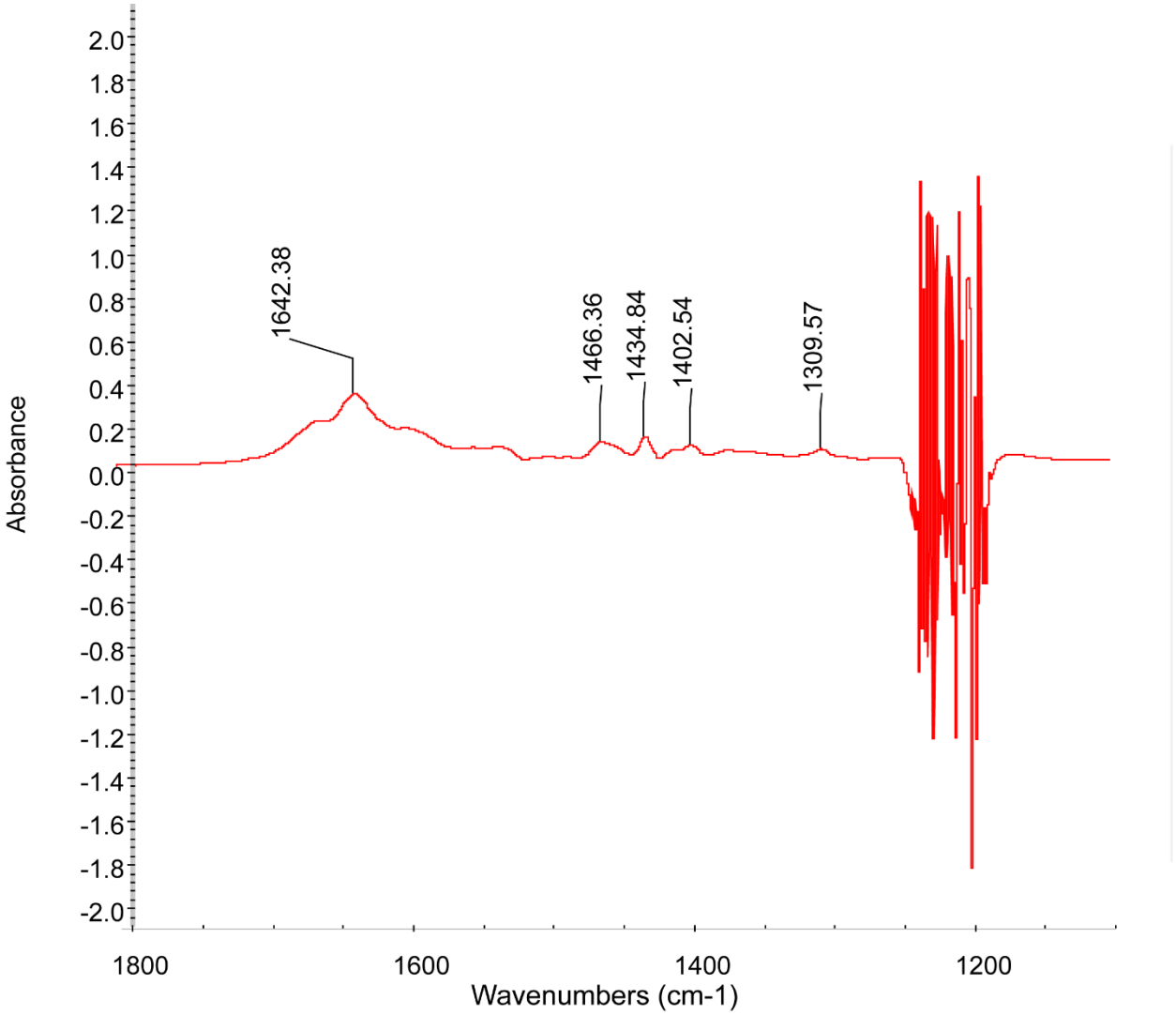

Figure S-8. IR absorbance spectrum of Figure **S-3E**, shrunk to fit on-scale. Dodecylguanidine free base (compound **2**), in water-saturated chloroform, vs. the same solvent, with additional independent subtractions of individual solvents to produce flatter baselines.

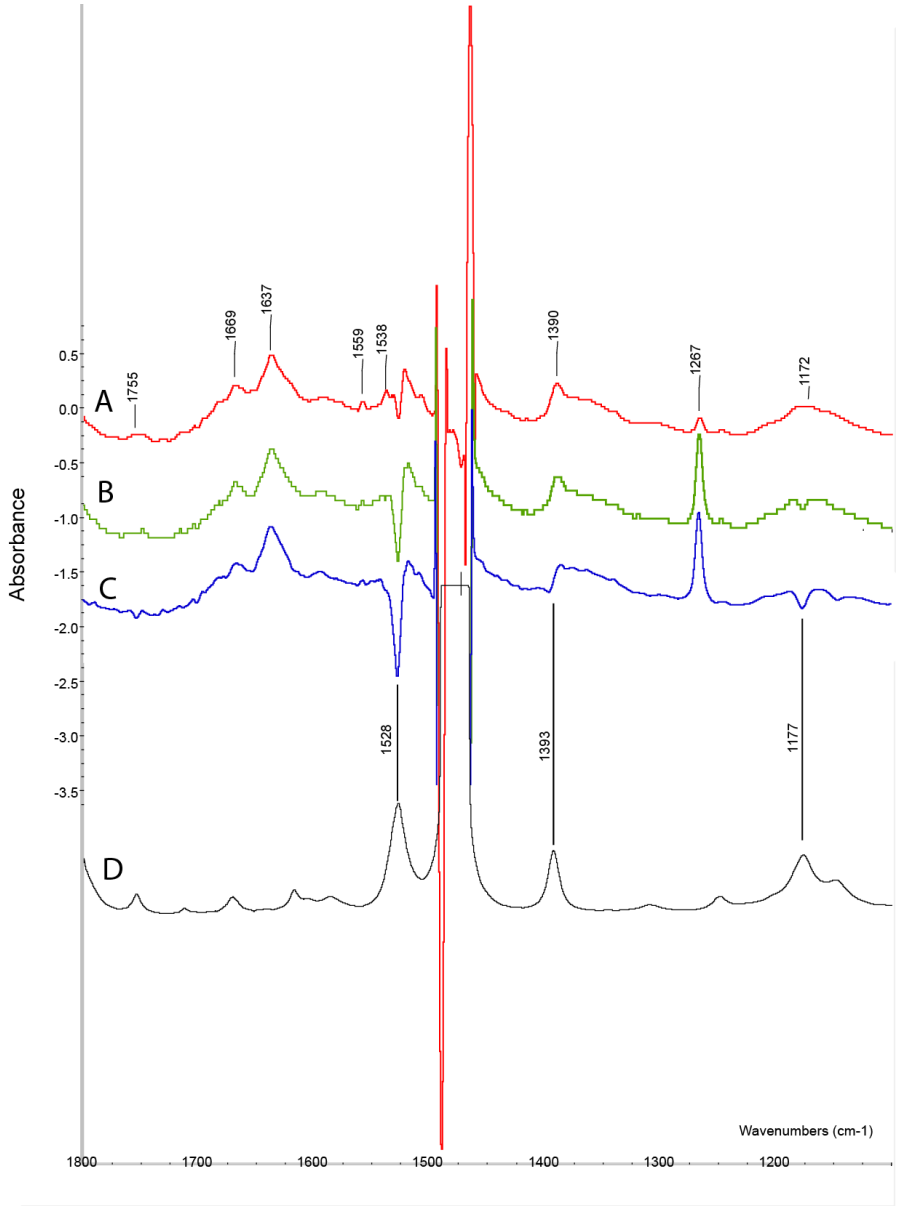

Figure S-9. **A**, IR absorbance spectrum of Figure **S-3G**, shrunk to fit on-scale, i.e. dodecylguanidine-$^{15}N_2$ free base (compound **2′**), in benzene, vs. the same solvent. **B**, **C,** same sample as **A**, measured 5 and 20 h subsequently, on the same scale but displaced vertically. All 3 spectra used the same neat benzene sample as background. The growing-in over time of the peak at 1267 cm^{-1} shows that this peak is due to a contaminant. There is a concomitant time-dependent increase in the size of negative peaks at 1528, 1393, and 1177 cm^{-1}, corresponding to absorbances measurable in pure benzene spectra (e.g., **D**). At the same time, peaks associated with the dodecylguanidine sample (e.g. 1637 cm^{-1}) barely change in size over the same time course. The simplest interpretation of this behavior is that dodecylguanidine catalyzes the conversion of benzene to a contaminant with a peak at 1266 cm^{-1}. This was never seen with the natural-abundance sample (Figure S-3A) because the higher concentrations available for it allowed much shorter measurement times, e.g. 1 h for Figure S-3A vs 4 h for Figure S-3G.

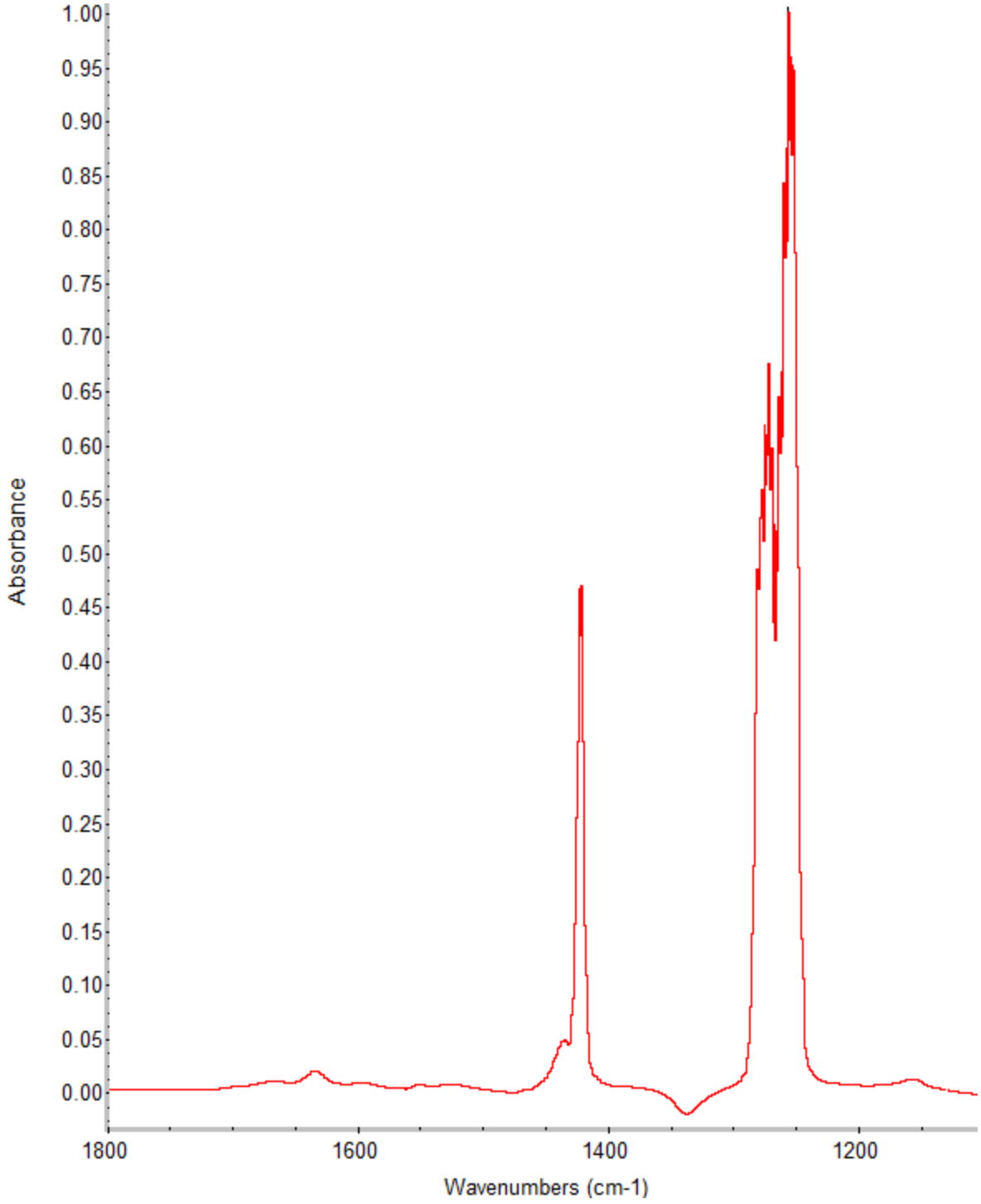

Figure S-10. IR absorbance spectrum of Figure **S-3I**, without blanking, shrunk to fit on-scale. Dodecylguanidine-$^{15}N_2$ free base (compound **2′**), in CH_2Cl_2, vs. the same solvent; with additional subtraction of the absorbance spectrum of the neat solvent, in order to produce the flattest possible baseline.

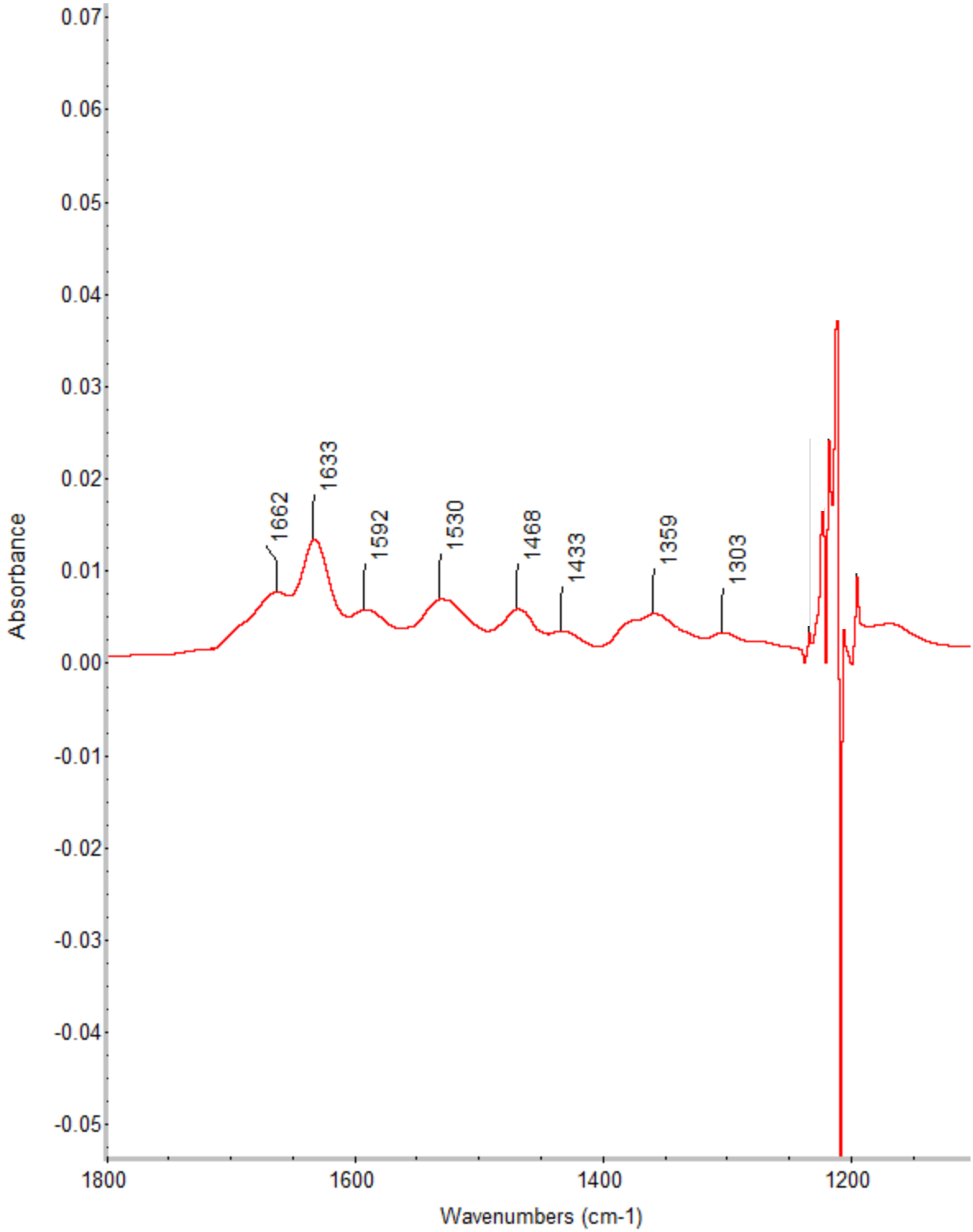

Figure S-11. IR absorbance spectrum of Figure **S-3J**, shrunk to fit on-scale. Dodecylguanidine-$^{15}N_2$ free base (compound **2′**), in chloroform ($CHCl_3$), vs. the same solvent. Additional subtraction of the absorbance spectrum of the neat solvent was then performed, in order to produce the flattest possible baseline.

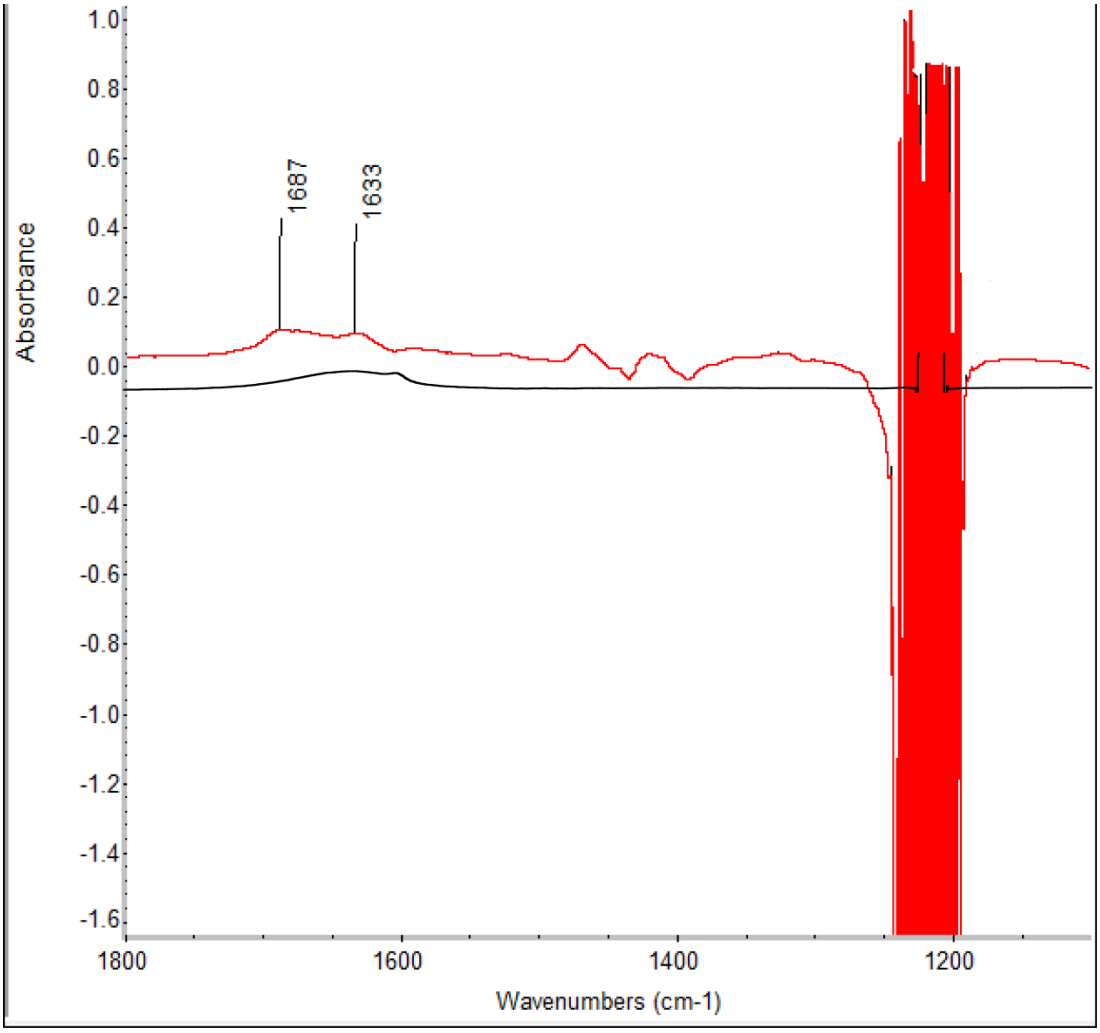

Figure S-12. IR absorbance spectrum of Figure **S-3K**, shrunk to fit on scale (red trace). Dodecylguanidine-$^{15}N_2$ free base (compound **2′**), in water-saturated chloroform, vs. the same solvent, with additional independent subtractions of individual solvents to produce flatter baselines. The regions near 1690, 1440, and 1390 cm^{-1} remain particularly uncertain because of a lack of confidence in these bandshapes, due to difficulties with subtraction of the multiple solvent absorbances near these regions. The black trace shows, with a small vertical displacement, the measured absorbance spectrum of 0.01% water in chloroform, vs dry chloroform. The greater breadth of this bandshape indicates that the peaks near 1687 and 1633 cm^{-1} in the red trace would not be removed by further subtraction of water absorption. However, there remains significant uncertainty in the exact shape and intensity in this region of the red spectrum, because the shape of the underlying water absorption band could be affected by the presence of the dodecylguanidine solute, i.e. it might not actually match the black trace. The subtraction of the water band to give a flat baseline was not as difficult for the natural-isotope-abundance dodecylguanidine (Fig. **S-8**), most likely because that solute was dissolved at a ~4-fold higher concentration (i.e. saturation), due to much greater amounts having been prepared.