HCN polymers characterized by SSNMR: Solid state reaction of crystalline tetramer (diaminomaleonitrile)

Irena Mamajanov^{a)} and Judith Herzfeld^{b)}*Department of Chemistry, Brandeis University, Waltham, Massachusetts 02454-9110, USA*

(Received 15 January 2009; accepted 7 February 2009; published online 1 April 2009)

The HCN tetramer, diaminomaleonitrile, crystallizes in sheets with amine and nitrile groups of neighboring molecules in close proximity. This suggests the possibility of relatively facile acid-base addition to form a protopeptide polymer. We find that moderate heating under argon indeed results in an unmistakable reaction, with the abrupt transformation of pale crystallites to shrunken dark particles that become electrically conductive upon doping with iodine. Since nearly a quarter of the mass is lost in the process and the released gas condenses, polymerizes, and reacts with aqueous AgNO₃ like HCN, it seems likely that the dark solid is a polymer of HCN trimer. ¹³C and ¹⁵N solid state NMR spectra show the formation of new N–C bonds, and entirely different functional groups from those observed in polymers formed by liquid HCN. These include three different types of nitrogen functionalities and an absence of saturated carbon or nitrile. The observed chemical shifts, optical properties, and electrical conductivity are consistent with polymers of HCN trimer that have undergone cyclization to form poly-[aminoimidazole]. © 2009 American Institute of Physics. [DOI: 10.1063/1.3092909]

I. INTRODUCTION

It has long been speculated that HCN polymers could have played an important role in prebiotic chemistry.^{1–5} One of most intriguing proposals,² based on observations of α -amino acids in polymer hydrolysates, suggests the formation of protopeptides by acid-base polymerization of the HCN trimer, aminomalononitrile. However, our previous NMR study⁶ showed that protopeptide is not formed in the polymerization of neat HCN. On the other hand, the same study showed that crystalline HCN tetramer, diaminomaleonitrile (DAMN) [Figs. 1(a)–1(c)] is formed as a side product. The formation of crystals is potentially significant because they comprise sheets of DAMN molecules with amine-nitrile hydrogen bonds that might be predisposed to acid-base addition.^{7–9} Such polymerization, followed by tautomerization and HCN release, might lead to Matthews' protopeptide (as illustrated in Fig. 1). Here we report an exploration of this hypothesis that finds that mild heating leads to a solid state reaction that we characterize by a variety of solid state NMR experiments, supplemented by stoichiometric and electrical conductivity measurements. In the NMR experiments, chemical shifts allow us to identify functional groups and dipolar interactions allow us to identify bond connectivities.

II. METHODS

A. Synthesis

Unlabeled DAMN (Aldrich) was recrystallized from isobutyl alcohol prior to use. Mixed-labeled DAMN was ex-

tracted with hot isobutyl alcohol from the mixture of DAMN and polymer that was formed by the base-catalyzed reaction of a 1:1 mixture of H¹³CN and HC¹⁵N described previously.⁶ Recrystallized DAMN was sealed in a pressure tube under argon and incubated at 125 °C for 12 h to assure complete conversion to polymer. For electrical conductivity measurements, the polymer was doped by exposure to iodine vapor for varying periods of time at room temperature.

B. Stoichiometry

A reaction flask containing recrystallized DAMN, was connected, via an evacuated transfer manifold, to a dry ice/acetone-cooled collection flask, containing a catalytic amount of triethylamine. After the system was evacuated, the reaction flask was heated to 125 °C for 3 h. After closing the valve on the collection flask, it was disconnected and incubated at 5 °C for 3 days.

C. Hydrolysis

Natural abundance polymer was incubated in 6*N* hydrochloric acid at 125 °C for 24 h.

D. Solid state NMR

Conventional use was made of cross polarization (CP) from ¹H's, to enhance ¹³C and ¹⁵N signals and accelerate acquisition, combined with magic angle spinning (MAS) and high power ¹H decoupling, to resolve signals. In addition, double cross polarization (DCP) spectra,¹⁰ entailing an additional transfer of polarization from ¹³C to ¹⁵N were used to assign the signals of ¹⁵N nuclei bound to ¹³C nuclei in mixed-labeled samples. For delay-without-decoupling (Dw/oD) spectra, ¹H decoupling was turned off between cross polarization and data acquisition to dephase signals

^{a)}Present address: School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, 30332.

^{b)}Author to whom correspondence should be addressed. Electronic mail: herzfeld@brandeis.edu.

FIG. 1. Hypothetical pathway to Matthews' protopeptide (Ref. 2) from DAMN via acid-base addition followed by release of HCN: [(a) and (b)] tautomers of DAMN; [(d) and (f)] tautomers of polymerized DAMN; [(g)–(m)] tautomers of polymerized HCN trimer including Matthews' protopeptide, **h**.

from nuclei bonded to ^1H .^{11,12} All spectra were acquired on a 360 MHz (^1H frequency) spectrometer (Cambridge Instruments), using a 4 mm MAS probe (Varian) operated at 10 kHz. Samples (typically 50 mg) were sealed under argon in rotor inserts purchased from Wilmad. The spectra were obtained with ramped amplitude Hartmann–Hahn cross polarization,^{13,14} TPPM ^1H decoupling during data acquisition,¹⁵ and 9 s recycle delays. Typical rf fields were 50 kHz for CP and 83 kHz for ^1H decoupling. CP contact times were 2 ms for ^{13}C and 5 ms for ^{15}N . The usual TPPM parameters were 170° for the pulse angle and 12° for the phase. For DCP, the ^{13}C -to- ^{15}N CP was optimized for single bond transfer using a standard glycine sample: with a constant amplitude field of 25 kHz, accompanied by 83 kHz cw ^1H decoupling, the contact time was 5 ms. For Dw/oD, a CPMAS echo sequence was used during the delay period to remove linear phase shifts.¹⁶ Best results were obtained with a delay of two rotor periods (200 ms).

E. Solution NMR

Single-pulse, ^1H -decoupled ^{13}C spectra were acquired on a Varian Inova spectrometer operating at 400 MHz ^1H frequency.

F. Fourier transform infrared

Precipitate was washed, dried, milled with KBr, and pressed into pellets. Spectra of pellets containing ~ 1 wt % sample were acquired on a Perkin-Elmer Spectrum BX Fourier transform infrared (FTIR) spectrometer.

G. Electrical conductivity measurements

Pulverized samples were compressed between two copper plates and the current was measured as a function of the applied dc voltage using a Beckman Industrial™ 4410 Ameter. The controls were recrystallized DAMN (no conductivity) and doped polypyrrole (Aldrich, 10–40 S/cm).

FIG. 2. (Color online) Recrystallized DAMN under argon, before (left) and after (right) heating.

III. RESULTS

Figure 2 shows the appearance of recrystallized DAMN before and after heating to 125°C in a pressure tube under argon. The reaction is not immediate, but it is abrupt, indicating either structural cooperativity, via the crystal lattice, or thermodynamic cooperativity, due to release of heat. Nevertheless, shrunken outlines of the original DAMN crystallites are visible in the dark, brittle product at the bottom of the tube. In addition, a dark film coats the upper walls of the tube. The latter is similar to the dark residues that are formed by HCN vapors. By repeating the reaction in a flask connected by an evacuated transfer manifold to a cold collection flask, we were able to determine that the released material does indeed behave like HCN in that it condenses to a white crystalline solid when cooled by dry ice/acetone, melts to a colorless liquid when warmed to 5°C , and forms a dark solid at the expected rate in the presence of catalytic base at 5°C . In addition, when collected over aqueous AgNO_3 , the released material forms a white precipitate that shows the distinctive signal of cyanide in the infrared. The stoichiometry of the reaction is summarized in Table I. Taken together, the results suggest that each HCN tetramer loses one HCN monomer per molecule upon polymerization.

Figure 3 compares ^{13}C CPMAS spectra of DAMN, DAMN polymer, and conventional HCN polymer (prepared as described previously⁶). In all cases, the narrow signals are due to crystalline DAMN and the broad signals are due to polymer. Focusing first on the narrow signals, we see that,

TABLE I. Stoichiometry results.

Trial	Initial mass DAMN (g)	Mass (DAMN) _x product (g)	Mass recovered (HCN) _x (g)
1	10.156	7.948	1.714
2	10.203	8.105	1.769
3	10.089	7.901	1.690

FIG. 3. CPMAS ^{13}C solid state NMR spectra of (a) natural abundance recrystallized DAMN (4480 scans), (b) the polymer obtained from the present thermally induced solid state reaction of DAMN (2688 scans), and (c) conventional HCN polymer obtained by the base-catalyzed reaction of neat HCN (2178 scans). Asterisks mark spinning sidebands.

whereas crystalline DAMN appears as a side product of HCN polymerization at 5 °C [Fig. 3(c)], DAMN is completely consumed by heating DAMN crystals at 125 °C [Fig. 3(b)]. From the broad signals in the spectra, we see that the polymer formed by heating crystalline DAMN is very different from the one formed by liquid HCN: whereas carbon in HCN polymer appears in both the upfield saturated region and the downfield unsaturated region [Fig. 3(c)], the DAMN polymer is characterized by a single broad downfield peak with a maximum at 157 ppm [Fig. 3(b)]. Of particular interest is the absence of detectable nitrile in the DAMN product. Nitrile carbons have unusually large chemical shift anisotropies, such that the isotropic signal at ~ 124 ppm is accompanied by a downfield spinning sideband that is nearly equally intense at our spinning frequency [as observed in Figs. 3(a) and 3(c)]. In the DAMN product [Fig. 3(b)], sidebands are absent.

Figure 4 shows a series of ^{15}N CPMAS spectra. Comparison of the CPMAS spectra of DAMN and DAMN polymer [Figs. 4(a) and 4(b)] shows once again that DAMN has been fully transformed on heating. In contrast to the ^{13}C spectrum of the DAMN polymer [Fig. 3(b)], the ^{15}N spectrum [Fig. 4(b)] shows three distinct sets of signals at ~ 234 , ~ 146 , and ~ 83 ppm. The ~ 234 ppm signal is clearly due to unsaturated nitrogen, while the ~ 146 and ~ 83 ppm signals are distinctive for pyrrole and ene-amine, respectively.

To learn more about these three functionalities, we used DCP spectroscopy to assign ^{15}N nuclei bonded to ^{13}C nuclei in a sample prepared from an equimolar mixture of H^{13}CN and HC^{15}N . Since the formation of DAMN from HCN involves no new C–N bonds, ^{13}C – ^{15}N pairs will be due exclu-

FIG. 4. CPMAS ^{15}N solid state NMR spectra of (a) recrystallized DAMN (4096 scans), (b) the polymer obtained from the present thermally induced solid state reaction of DAMN (5120 scans), (c) the polymer with mixed labels (see text) after double cross polarization (10240 scans), and (d) the polymer after a Dw/oD (5760 scans).

sively to bonds formed during the polymerization of DAMN. Comparison of the DCP spectrum in Fig. 4(c) with the CP spectrum in Fig. 4(b), clearly shows that a substantial part of the most downfield nitrogen signal, at 234 ppm, must be due to such a nitrogen. This is consistent with the absence of

nitrile signals in the ^{13}C spectrum. At the same time, only a very much smaller fraction of the nitrogen signals, at ~ 146 and ~ 83 ppm are selected by DCP, suggesting that these signals are primarily due to nitrogens that are not bonded to a second carbon or that dynamics are interfering with DCP.

Further insight into the various nitrogen functionalities can be obtained by imposing a Dw/oD before data acquisition. This causes the protonated nitrogens to become dephased, leaving signals only from nitrogens that are not strongly coupled to protons. Comparison of the relative intensities in the Dw/oD spectrum in Fig. 4(d) with those in the CP spectrum in Fig. 4(b), shows that much of the most upfield signal (at ~ 83 ppm) is dephased, as expected for an amine. Of greater interest, is the survival of the other two nitrogen signals, which indicates that they represent nitrogens that are either unprotonated or tautomerizing rapidly enough to average their dipole interaction with protons to zero.

No conditions were found under which the DAMN polymer could be dissolved and the results of attempting hydroly-

FIG. 5. Intrapolymer cyclization by the side chain imines of structures **i**, **j**, and **m** (Fig. 1) to give polyaminoimidazole (**n-r**).

sis proved uninteresting: the residual solid showed no change in the solid state ^{13}C spectrum and the supernatant yielded no solution ^{13}C signal.

The fresh DAMN polymer had no detectable electrical conductivity. However, electrical conductivity was observed after exposure to iodine vapor at room temperature. The maximum conductivity reading, obtained after 3 h of exposure, was about 100-fold lower than that of doped polypyrrole (10–40 S/cm).

IV. DISCUSSION

An early study of DAMN (Ref. 17) mentioned the formation of a dark product in the course of melting point measurements. The present experiments show that

- (1) this reaction also occurs under argon (Fig. 2),
- (2) HCN is released in an amount approaching 1 molecule per molecule of DAMN (Table I), and
- (3) a new N–C bond is formed by at least one of the three remaining nitrogens [Fig. 4(c)].

This much is consistent with the hypothesis laid out in Fig. 1. However, other results are not consistent with the hypothesis. None of the polymers in Fig. 1 is expected to be dark or electrically conductive on doping. Furthermore, the structures **g**, **h**, **k**, and **l** can all be specifically excluded by the absence of nitrile NMR signals. In addition, the absence of upfield ^{13}C resonances in Fig. 3(b) excludes the presence of structures **h**, **k**, and **l** which each have a sp^3 carbon.

The remaining tautomers in Fig. 1 (structures **i**, **j**, and **m**) are expected to be reactive toward cyclization or cross-linking. Two possible reactions, one intrapolymer and one interpolymer, are shown in Figs. 5 and 6. Of the resulting structures, **o** is most consistent with the experimental observations:

- (a) Dark color and conductivity on doping. Only structure **o** has an extended π -system.
- (b) Ene-amine (^{15}N signal at ~ 83 ppm). All the structures except **p** have this feature.
- (c) Pyrrole (^{15}N signal at ~ 146 ppm). Only structures **n** and **o** have this feature. Whereas, free imidazole and

FIG. 6. Interpolymer cross-linking by the protonated imines in structure **j** (Fig. 1).

histidine tautomerize too rapidly in solution to show a distinct pyrrole signal, bias in favor of one tautomer is seen in histidine in the solid state and even in adenine in solution. In the present system, bias toward structure **o** is expected due to stabilization by the extended π -system cited above.

- (d) Absence of saturated carbons (empty upfield ^{13}C spectrum). All the structures except **p** and **r** conform in this respect.
- (e) DCP. Like structures **g–m**, structure **s** has only one N–C bond between HCN trimers. However, weak DCP is observed at ~ 146 ppm and, as noted above, since DCP can be defeated by dynamics (such as the tautomerism expected in our systems), it is better for demonstrating the presence of a C–N bond than the absence of one.
- (f) Dw/oD. Only structures **p**, **q**, and **r** have two deprotonated nitrogens. However, the chemical shifts of these nitrogens will be similar to each other and far downfield. Therefore, survival of the ~ 146 ppm (most likely pyrrole) signal must be due to sufficiently rapid proton exchange to prevent dephasing of the nitrogen (without averaging the signals of the two ring nitrogens).

V. CONCLUSIONS

In its crystal lattice, DAMN is poised for acid-base polymerization with the potential to form Matthews' protopeptide² upon the release of one HCN molecule per DAMN unit. Consistent with this hypothesis, we have found that a new N–C bond is formed upon mild heating and nearly a quarter of the mass is released as HCN. However, the apparent polymer of trimers is dark, electrically conductive on doping, and resistant to hydrolysis. Furthermore, ^{13}C solid state NMR shows that no nitrile survives. Instead the ^{15}N solid state NMR shows evidence of ene-amine and pyrrole.

Taken together, the experimental results suggest that, at 125 °C, Matthews' proposed protopeptide is not stable relative to intrapolymer cyclization to form poly-[amino-imidazole].

ACKNOWLEDGMENTS

The NMR spectra were acquired at the MIT-Harvard Center for Magnetic Resonance supported by the NIH under Grant No. EB002026. We also thank Barry Snider for suggesting the scheme in Fig. 5, Marina Belenky for the FTIR analysis, and Robert Griffin for helpful discussions. Financial support was provided by the NIH under Grant No. R01EB002175 and NASA Grant No. NNX07AV52G.

¹R. D. Minard, W. Yang, P. Varma, J. Nelson, and C. N. Matthews, *Science* **190**, 387 (1975).

²C. N. Matthews and R. E. Moser, *Proc. Natl. Acad. Sci. U.S.A.* **56**, 1087 (1966).

³J. P. Ferris and W. J. Hagan, *Tetrahedron* **40**, 1093 (1984).

⁴J. P. Ferris, E. H. Edelson, J. M. Auyeung, and P. C. Joshi, *J. Mol. Evol.* **17**, 69 (1981).

⁵J. P. Ferris, P. C. Joshi, E. H. Edelson, and J. G. Lawless, *J. Mol. Evol.* **11**, 293 (1978).

⁶I. Mamajanov and J. Herzfeld *J. Chem. Phys.* **130**, 134503 (2009).

⁷B. R. Penfold and W. N. Lipscomb, *Acta Crystallogr.* **14**, 589 (1961).

⁸Y. Yamada, N. Nagashimi, Y. Iwashita, A. Nakamura, and I. Kumashir, *Tetrahedron Lett.* **9**, 4529 (1968).

⁹A. A. Sidorov, I. G. Fomina, V. V. Nesterov, S. E. Nefedov, I. L. Eremenko, and I. I. Moiseev, *Russ. Chem. Bull.* **48**, 573 (1999).

¹⁰J. Schaefer, R. A. McKay, and E. O. Stejskal, *J. Magn. Reson.* **34**, 443 (1979).

¹¹S. J. Opella, M. H. Frey, and T. A. Cross, *J. Am. Chem. Soc.* **101**, 5856 (1979).

¹²S. J. Opella and M. H. Frey, *J. Am. Chem. Soc.* **101**, 5854 (1979).

¹³S. R. Hartmann and E. L. Hahn, *Phys. Rev.* **128**, 2042 (1962).

¹⁴A. Pines, M. G. Gibby, and J. S. Waugh, *J. Chem. Phys.* **59**, 569 (1973).

¹⁵A. E. Bennett, C. M. Rienstra, M. Auger, K. V. Lakshmi, and R. G. Griffin, *J. Chem. Phys.* **103**, 6951 (1995).

¹⁶M. G. Munowitz, R. G. Griffin, G. Bodenhausen, and T. H. Huang, *J. Am. Chem. Soc.* **103**, 2529 (1981).

¹⁷C. Bedel, *C. R. Hebd. Seances Acad. Sci.* **176**, 168 (1923).