Interstellar Formation of Nitrogen Heteroaromatics [Indole, C_8H_7N; Pyrrole, C_4H_5N; Aniline, $C_6H_5NH_2$]: Key Precursors to Amino Acids and Nucleobases

Jia Wang, Anatoliy A. Nikolayev, Joshua H. Marks, Andrew M. Turner, Sankhabrata Chandra, N. Fabian Kleimeier, Leslie A. Young, Alexander M. Mebel,* and Ralf I. Kaiser*

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Nitrogen-substituted polycyclic aromatic hydrocarbons (NPAHs) are not only fundamental building blocks in the prebiotic synthesis of vital biomolecules such as amino acids and nucleobases of DNA and RNA but also a potential source of the prominent unidentified 6.2 μm interstellar absorption band. Although NPAHs have been detected in meteorites and are believed to be ubiquitous in the universe, their formation mechanisms in deep space have remained largely elusive. Here, we report the first bottom-up formation pathways to the simplest prototype of NPAHs, indole (C_8H_7N), along with its building blocks pyrrole (C_4H_5N) and aniline ($C_6H_5NH_2$) in low-temperature model interstellar ices composed of acetylene (C_2H_2) and ammonia (NH_3). Utilizing the isomer-selective techniques of resonance-enhanced multiphoton ionization and tunable vacuum ultraviolet photoionization reflectron time-of-flight mass spectrometry, indole, pyrrole, and aniline were identified in the gas phase, suggesting that they are promising candidates for future astronomical searches in star-forming regions. Our laboratory experiments utilizing infrared spectroscopy and mass spectrometry in tandem with electronic structure calculations reveal critical insights into the reaction pathways toward NPAHs and their precursors, thus advancing our fundamental understanding of the interstellar formation of aromatic proteinogenic amino acids and nucleobases, key classes of molecules central to the *Origins of Life*.
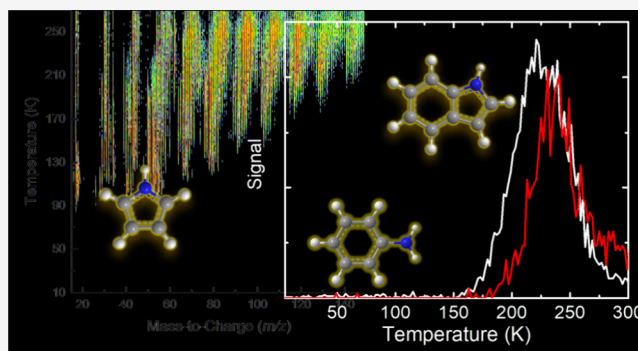
INTRODUCTION

Since the discovery of the cyano radical (CN) in the interstellar medium (ISM) in 1940 by McKellar,[1] nitrogen-containing molecules have attracted extensive attention from the astrochemistry,[2−5] physical chemistry,[6−10] and astrobiology communities[11,12] due to their vital role in the formation of organics in deep space linked to the *Origins of Life*.[13−16] *Origins of Life* explores the fundamental processes by which molecular building blocks of life have arisen from simple precursor molecules such as water (H_2O), carbon monoxide (CO), methane (CH_4), and ammonia (NH_3) condensed on interstellar nanoparticles that comprise molecular clouds.[12,17,18] Complex organic molecules can be produced in interstellar ices via energetic nonequilibrium reactions triggered by vacuum ultraviolet (VUV) light and galactic cosmic rays (GCRs).[19] Nitrogen-containing molecules in particular account for nearly one-third of some 300 molecules identified in the ISM; these can be classified as nitriles (RC≡N), amines (RNR′R″), imines (RC=NR′), and amides (RCONHR′) with R, R′, and R″ being organic groups.[20,21] The recent detection of aromatic nitriles such as benzonitrile (C_6H_5CN), cyanonaphthalenes ($C_{10}H_7CN$), and 2-cyanoin-

dene (C_9H_7CN)[22−24] in the Taurus Molecular Cloud (TMC-1) carrying the benzene (C_6H_6, **1**), naphthalene ($C_{10}H_8$), and indene (C_9H_8) moieties, respectively, suggested future astronomical searches for nitrogen-substituted polycyclic aromatic hydrocarbons (NPAHs)—polycyclic aromatic hydrocarbons (PAHs) in which one or more CH moieties are formally replaced by isoelectronic nitrogen atom(s). NPAHs are recognized as key precursors to biorelevant molecules such as the proteinogenic amino acid tryptophan ($C_{11}H_{12}N_2O_2$) along with nucleobases[25] and play a fundamental role in the abiotic synthesis of vital biomolecules in deep space,[26] eventually contributing to the molecular *Origins of Life* on early Earth through their exogenous delivery.[27]
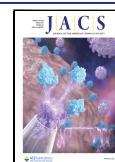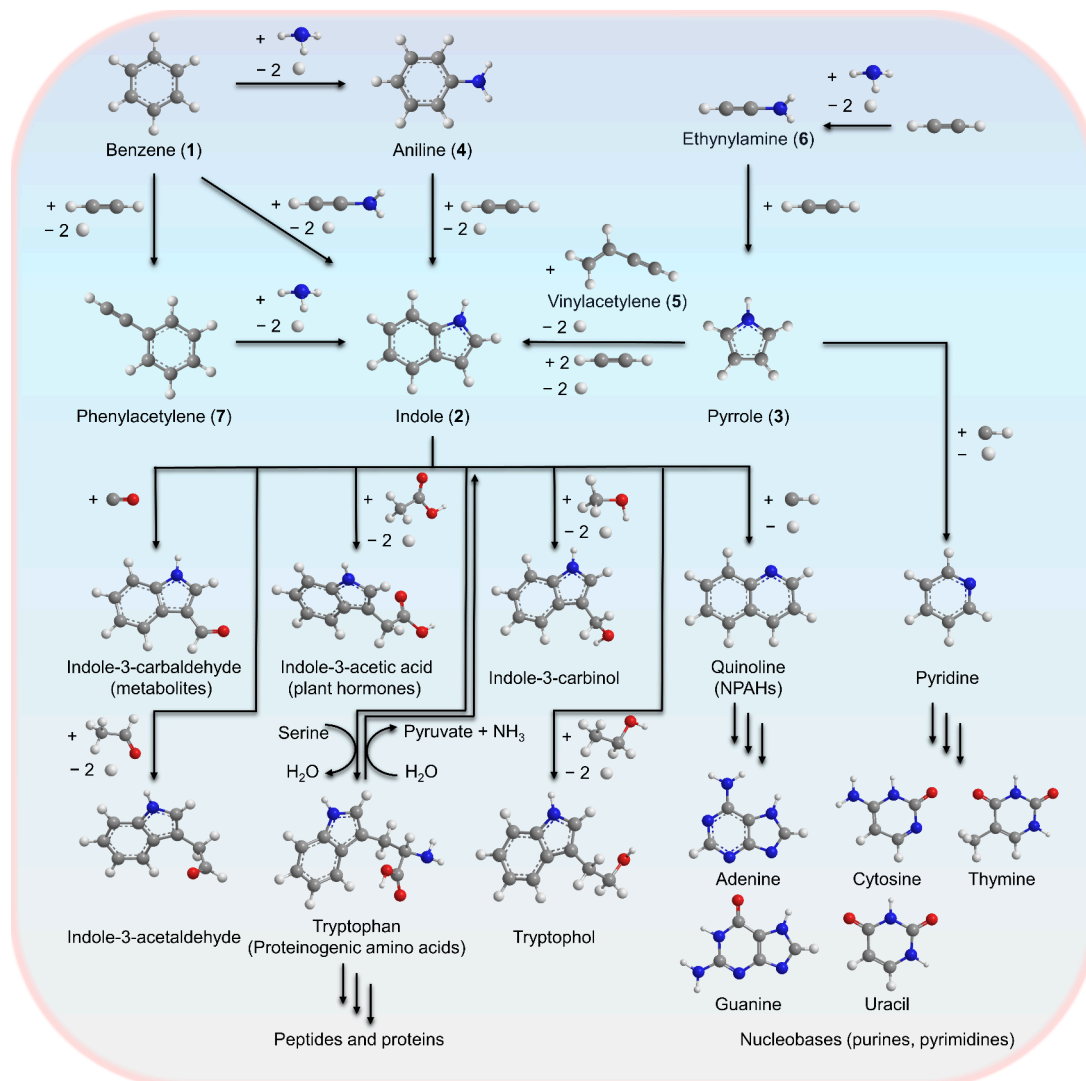
Figure 1. Proposed interstellar formation of nitrogen heteroaromatics indole, pyrrole, and aniline. The preparation of indole (C_8H_7N, **2**), pyrrole (C_4H_5N, **3**), and aniline ($C_6H_5NH_2$, **4**) is accomplished in interstellar analog ices containing acetylene and ammonia via energetic processing by simulated galactic cosmic rays. Indole (**2**) and pyrrole (**3**) as precursors may react with interstellar molecules to form critical biomolecules including indole-3-carbaldehyde, indole-3-acetaldehyde, plant hormones (indole-3-acetic acid), proteinogenic amino acid tryptophan, indole-3-carbinol, tryptophol, NPAHs (quinoline), and pyridine.

Although no individual NPAH has yet been identified in the gas phase in the ISM,[20] their presence has been inferred from the prominent unidentified infrared (UIR) feature (6.2 μm band), which closely matches the characteristic vibrational frequencies of the aromatic carbon−carbon stretch of NPAHs.[28,29] NPAHs such as (iso)quinolines (C_9H_7N) have also been detected in the Murchison meteorite[30] thus documenting a hitherto unidentified extraterrestrial source of NPAHs, potentially on the ice-coated interstellar nanoparticles that compose.[31] However, despite remarkable progress toward an understanding of the elementary gas-phase reactions leading to PAHs in interstellar and circumstellar environments, the unraveling of the fundamental formation mechanisms of their nitrogen-substituted counterparts (NPAHs) has just scratched the surface[13,27,32,33] with the formation mechanism of even the simplest prototypes such as indole (C_8H_7N, **2**) along with their molecular building blocks such as pyrrole (C_4H_5N, **3**) having remained elusive as of now.

In prebiotic chemistry, indole (**2**) and pyrrole (**3**) formed in interstellar ices could react further to form vital biomolecules (Figure 1) through energetic, nonequilibrium reactions initiated by GCRs eventually leading to peptides and nucleobases of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Reactions of indole (**2**) with carbon monoxide (CO) or acetaldehyde (CH_3CHO) could eventually synthesize biologically active metabolites indole-3-carbaldehyde (C_9H_7NO) or indole-3-acetaldehyde ($C_{10}H_9NO$), respectively. The plant hormones such as indole-3-acetic acid ($C_{10}H_9NO_2$) may be accessed through the reaction of indole (**2**) with acetic acid (CH_3COOH). Also, indole (**2**) serves as the chromophore of the proteinogenic amino acid tryptophan, which can be prepared through the reaction of indole (**2**) with the amino acid serine ($C_3H_7NO_3$).[34] Likewise, the reaction of indole (**2**) with methanol (CH_3OH) and ethanol (CH_3CH_2OH) might prepare indole-3-carbinol (C_9H_9NO) and tryptophol ($C_{10}H_{11}NO$), respectively. In addition, as the simplest prototype of NPAHs, indole (**2**) acts as a key precursor to complex NPAHs such as (iso)quinolines (C_9H_7N) via molecular mass growth processes. Further, pyrrole (**3**), the five-membered substituent cycle of indole (**2**), participates in

the synthesis of porphyrins[35] and reacts with the methylidyne (CH) radical in the gas phase to form pyridine (C_5H_5N),[36] which, along with NPAHs, can synthesize nucleobases (purines, pyrimidines) (Figure 1). Therefore, the unraveling of the abiotic formation mechanisms of indole (**2**) and pyrrole (**3**) is of fundamental importance to the astrobiology and astrochemistry communities to rationalize the origin and formation pathways of key biomolecules such as amino acids and nucleobases in space.

Here, we report the first bottom-up synthesis of indole (C_8H_7N, **2**)—a fundamental molecular building block of the proteinogenic amino acid tryptophan—together with pyrrole (C_4H_5N, **3**) and aniline ($C_6H_5NH_2$, **4**) as its precursors in interstellar model ices. This is accomplished in low-temperature acetylene and ammonia (C_2H_2–NH_3) ices at 5 K exposed to energetic electrons, simulating the GCR exposure of interstellar ices in cold molecular clouds aged up to 2×10^7 years.[37] The electron kinetic energies of 5 keV was used because its linear energy transfer is comparable to that of 10–20 MeV GCR protons deposit into ices.[38,39] Utilizing resonance-enhanced multiphoton ionization (REMPI) and tunable vacuum ultraviolet (VUV) single-photon ionization (SPI) reflectron time-of-flight mass spectrometry (ReToF-MS), these molecules were *isomer-selectively* identified in the gas phase during temperature-programmed desorption (TPD) of the irradiated ices; this simulates the transition of a cold molecular cloud toward star formation. Our electronic structure calculations identify crucial routes leading to these aromatics (Figure 1) thus providing critical insights into the intrinsic nonequilibrium formation pathways of indole (**2**) along with the pyrrole (**3**) and aniline (**4**) precursors in interstellar ices. Acetylene is a major product of the photolysis and radiolysis of interstellar methane ices[40] and ammonia is a ubiquitous and critical constituent of interstellar ices with abundances up to 15% with respect to water,[41] the acetylene–ammonia ices selected in our laboratory simulations present a model ice to understand the formation pathways of indole (**2**), pyrrole (**3**), and aniline (**4**) in a comprehensive way. It is therefore anticipated that indole (**2**), pyrrole (**3**), and aniline (**4**) can be synthesized in interstellar ices bearing acetylene and ammonia in cold molecular clouds due to exposure to ionizing radiation such as GCRs. Upon gravitational collapse of the parent molecular cloud during star formation, ices containing these species can be ultimately incorporated into circumstellar disks; this matter contains the raw materials from which planets, planetoids, and comets form.[42,43] Consequently, molecules originally synthesized in interstellar ices may eventually be integrated into the matter of solar systems, such as our own. These organics may have been delivered to newly forming planets such as the early Earth by comets and meteorites, providing a plausible source of prebiotic molecules[44] and molecular precursors to critical biomolecules, thus playing a crucial role in the molecular *Origins of Life*.[45]

■ RESULTS

Infrared Spectroscopy. The Fourier transform infrared (FTIR) spectra of the acetylene–ammonia (C_2H_2–NH_3) ices before and after irradiation are dominated by the fundamental vibrational modes of acetylene (ν_3, 3236 cm^{-1}; ν_2, 1947 cm^{-1}; ν_5, 753 cm^{-1}) and ammonia (ν_3, 3380 cm^{-1}; ν_1, 3165 cm^{-1}; ν_4, 1629 cm^{-1}; ν_2, 1087 cm^{-1}) as well as the combination mode ($\nu_4 + \nu_5$, 1375 cm^{-1}) of acetylene and the overtone of ammonia ($2\nu_4$, 3303 cm^{-1}).[46–49] After irradiation, several weak

bands appear including the CH stretching modes at 2792 cm^{-1}, the C=C=N stretching mode at 2054 cm^{-1} and the NH bending mode at 1274 cm^{-1} (Figure 2, Table S1).[50,51]
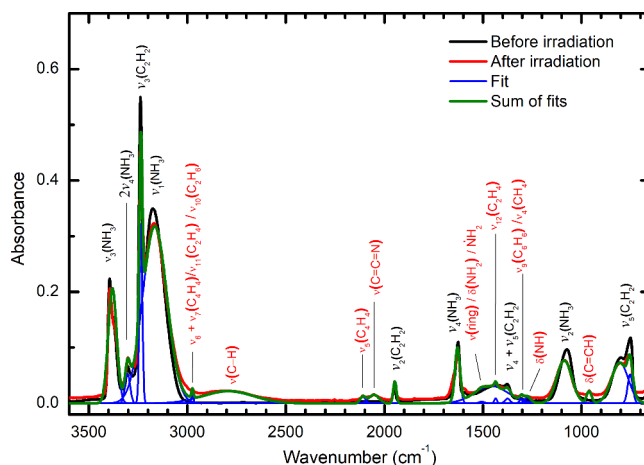

Figure 2. FTIR spectra of C_2H_2–NH_3 ice at 5 K before (black) and after (red) electron irradiation at a current of 100 nA for 60 min. Details of the assignments are listed in Table S1.

The absorption at 2974 cm^{-1} can be assigned to the combination mode of vinylacetylene (C_4H_4, **5**; $\nu_6 + \nu_7$), CH$_2$ symmetric stretch of ethylene (C_2H_4, ν_{11}) and/or CH$_3$ degenerate stretch of ethane (C_2H_6, ν_{10}).[47,52] The formation of vinylacetylene and ethylene can be further confirmed by absorptions at 2109 cm^{-1} (C_4H_4, ν_5) and 1435 cm^{-1} (C_2H_4, ν_{12}), respectively.[53,54] The absorption at 1506 cm^{-1} can be assigned to the ring vibration and/or the NH bending mode of pyrroles.[51,55] In addition, this feature may also link to amino (NH$_2$) radical, of which the infrared fundamental (ν_2) was measured at 1499 cm^{-1} in a nitrogen matrix.[56] The absorption at 1304 cm^{-1} is associated with the ring stretching mode of benzene (ν_9) and/or the deformation mode of methane.[57,58] Moreover, the absorption at 961 cm^{-1} links to the out-of-plane aromatic CH deformation of (substituted) benzenes.[59] However, due to the overlapping IR features of functional groups of complex organics formed during radiation exposure, infrared spectroscopy cannot unambiguously identify *individual complex organic molecules*, thus highlighting the necessity for an alternative analytical technique to *isomer-selectively* detect the desired products.

SPI-ReToF-MS and REMPI-ReToF-MS. Photoionization reflectron time-of-flight mass spectrometry (PI-ReToF-MS) has proven as a powerful tool to identify individual molecules in the gas phase.[18] It affords an isomer-specific identification upon single photon ionization (SPI) based on their adiabatic ionization energies (IEs; SPI-ReToF-MS) or with resonance-enhanced multiphoton ionization (REMPI) through isomer-specific resonance lines (REMPI-ReToF-MS).[18,59,60] At a photon energy of 10.49 eV, the target molecules pyrrole (C_4H_5N, IE = 8.207 ± 0.005 eV), aniline (C_6H_7N, IE = 7.720 ± 0.002 eV), and indole (C_8H_7N, IE = 7.7602 ± 0.0006 eV) can all be ionized.[61] This results in ion signals at m/z = 67, 93, and 117, respectively, in the TPD phase (Figure S1, Figures 3 and 4). To confirm the molecular formulas, it is imperative to exploit isotopically labeled ice mixtures such as $^{13}C_2H_2$–NH_3, C_2H_2–$^{15}NH_3$, and $^{13}C_2H_2$–$^{15}NH_3$ so that the m/z shifts in a readily predictable way.
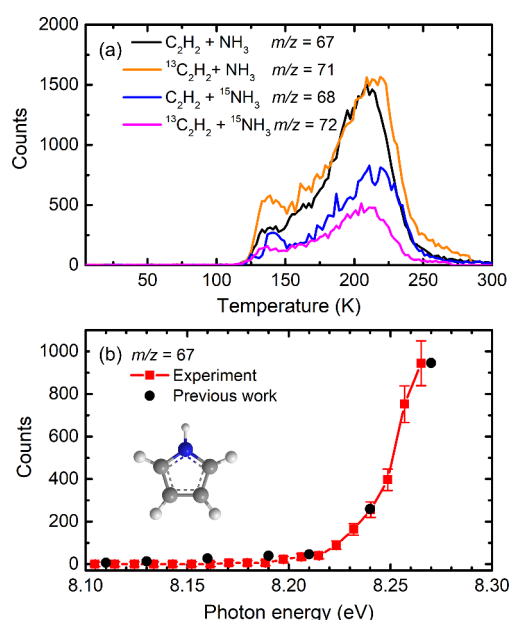
Figure 3. Ion signals during TPD of acetylene−ammonia ices and photoionization efficiency (PIE) curves. (a) TPD profiles were recorded at 10.49 eV from irradiated C_2H_2−NH_3 (m/z = 67), $^{13}C_2H_2$−NH_3 (m/z = 71), C_2H_2−$^{15}NH_3$ (m/z = 68), and $^{13}C_2H_2$−$^{15}NH_3$ (m/z = 72) ices, confirming the formula C_4H_5N. (b) The PIE curve measured at m/z = 67 (red) is plotted as a function of photon energy after correction for photon flux and TPD profile measured from 125 to 161 K. The reported reference PIE curve of pyrrole (black dots) was scaled to compare with the experimental results.

Pyrrole. The TPD profile of m/z = 67 exhibits a sublimation event between 120 and 275 K (Figure 3a). This ion signal can be associated with the molecular formulas C_2HN_3, $C_3H_3N_2$, C_4H_5N, and/or C_5H_7. The TPD profile shifts by 4 atomic mass unit (amu) (m/z = 71) in irradiated $^{13}C_2H_2$−NH_3 ice, by 1 amu (m/z = 68) in irradiated C_2H_2−$^{15}NH_3$ ice, and by 5 amu (m/z = 72) in irradiated $^{13}C_2H_2$−$^{15}NH_3$ ice indicating the presence of four carbon atoms and a single nitrogen atom, and hence the molecular formula C_4H_5N. Photoionization efficiency (PIE) curves, which report the intensity of ion counts at, e.g., m/z = 67, versus the photon energy, are collected in the TPD phase and compared to the PIE reference data.[62,63] Here, during the TPD of irradiated C_2H_2−NH_3 ice, the PIE was collected over a photon energy range of 8.10−8.27 eV (Figure 3b). The experimental data correlates nicely with the PIE reference curve of pyrrole (**3**)[63] thus demonstrating the formation of pyrrole (**3**). Also, the onset of ionization is determined to be 8.20 ± 0.01 eV, which is in good agreement with the previously determined IE of pyrrole (IE = 8.207 ± 0.005 eV).[61] An additional experiment was carried out at 7.90 eV, at which pyrrole (IE = 8.207 ± 0.005 eV) cannot be ionized. Compared with the result of m/z = 67 recorded at 10.49 eV in irradiated C_2H_2−NH_3 ice, the early sublimation event disappeared at 7.90 eV (Figure S2), providing further evidence for the formation of pyrrole (**3**).

Aniline and Indole. Figure 4 shows TPD profiles of m/z = 93 and m/z = 117 in processed C_2H_2−NH_3 ices recorded at 10.49 eV. The ion signal at m/z = 93 can be associated with the molecular formulas C_3HN_4, $C_4H_3N_3$, $C_5H_5N_2$, C_6H_7N, and/or C_7H_9. This TPD profile shifts by 6 amu (m/z = 99) in irradiated $^{13}C_2H_2$−NH_3 ice, by 1 amu (m/z = 94) in irradiated C_2H_2−$^{15}NH_3$ ice, and by 7 amu (m/z = 100) in irradiated $^{13}C_2H_2$−$^{15}NH_3$ ice (Figure 4a), indicating the presence of six carbon atoms and a single nitrogen atom. Therefore, the sublimation event at m/z = 93 can be clearly associated with a molecule of the molecular formula C_6H_7N. Similarly, the TPD
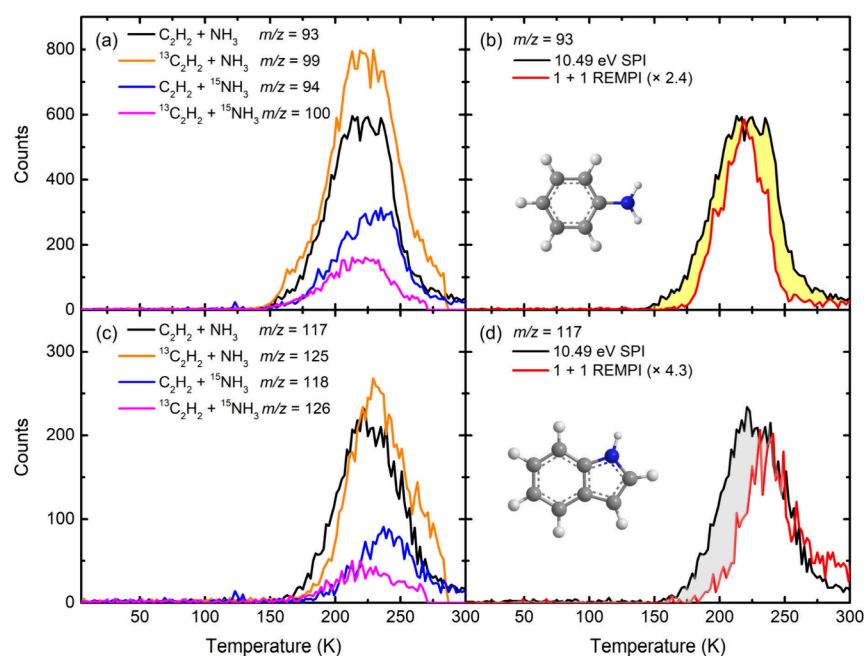

Figure 4. Ion signals during the TPD of acetylene−ammonia ices along with [1 + 1] REMPI data. TPD profiles were recorded at 10.49 eV from irradiated C_2H_2−NH_3, $^{13}C_2H_2$−NH_3, C_2H_2−$^{15}NH_3$, and $^{13}C_2H_2$−$^{15}NH_3$ ices confirming the formulas C_6H_7N (a) and C_8H_7N (c). Overlay of SPI (10.49 eV) and REMPI ion signals versus temperature for aniline recorded at 293.842 nm (b) and indole recorded at 283.817 nm (d). The shaded regions in yellow (b) and gray (d) indicate the sublimation events of structural isomers of aniline (**4**) and indole (**2**), respectively.
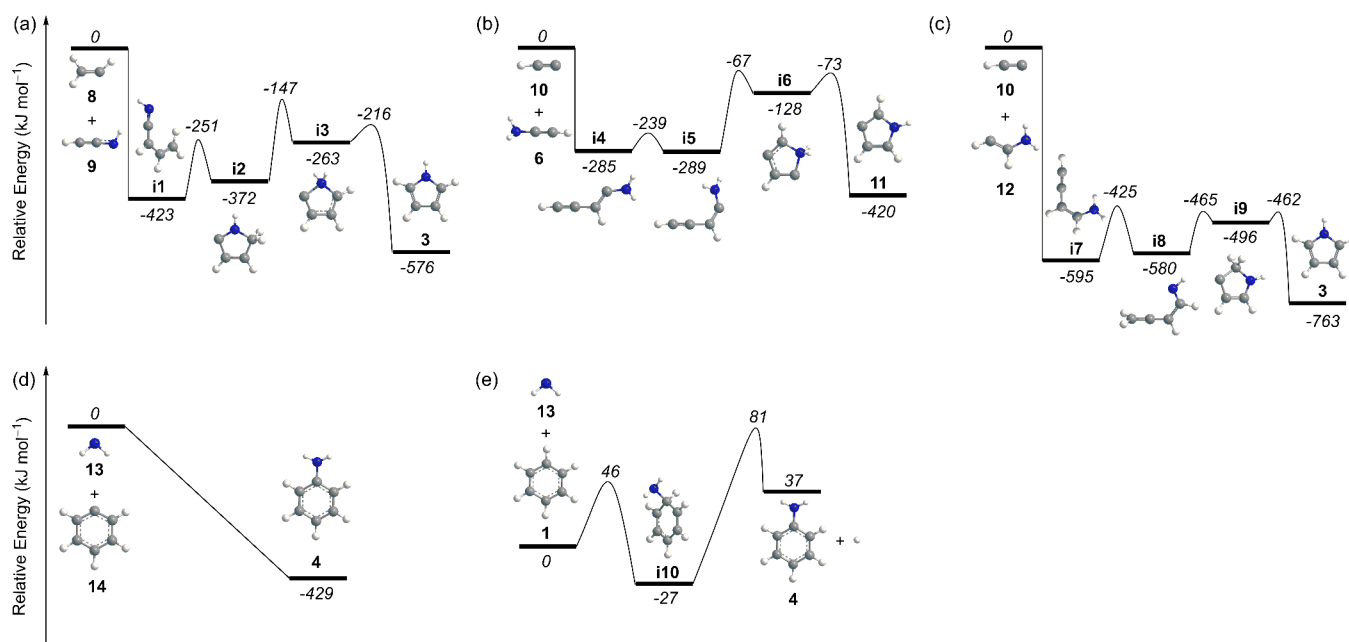
Figure 5. Potential energy surfaces leading to the formation of pyrrole (**3**) and aniline (**4**). Three barrierless (submerged barrier) reactions leading to pyrrole (**3**) are depicted: vinyl (CH$_2$CH, **8**) plus ethynylamidogen (HCCNH, **9**) (a), ethynyl (HCC, **10**) plus ethynamine (**6**) (b), and the ethynyl (**10**) plus 2-aminoethenyl (NH$_2$CHCH, **12**) (c). Two reactions leading to aniline (**4**) are depicted: amino (NH$_2$, **13**) plus phenyl (C$_6$H$_5$, **14**) (d), and amino (**13**) plus benzene (**1**) (e). The energies (italics) were computed at the CCSD(T)-F12/cc-pVTZ-F12//ωB97X-D/6-311G(d,p) level of theory. Atoms are colored in black (carbon), gray (hydrogen), and blue (nitrogen).

profile at m/z = 117 shifts by 8 amu (m/z = 125) in irradiated ^{13}C$_2$H$_2$–NH$_3$ ice, by 1 amu (m/z = 118) in irradiated C$_2$H$_2$–^{15}NH$_3$ ice, and by 9 (m/z = 126) amu in irradiated ^{13}C$_2$H$_2$–^{15}NH$_3$ ice (Figure 4c), suggesting the presence of eight carbon atoms and of a single nitrogen atom thus confirming its molecular formula to be C$_8$H$_7$N. Note that the TPD profiles may be shifted in isotopically labeled ices due to the differences in the desorption energies for isotopically labeled isomers and the reaction rates leading to their formation. It is important to highlight that both formulas C$_6$H$_7$N and C$_8$H$_7$N can represent multiple structural isomers that can also be ionized at 10.49 eV. Considering a significant overlap of the IE ranges of multiple isomers, it is difficult to identify individual C$_6$H$_7$N or C$_8$H$_7$N isomers by SPI-ReToF-MS alone.

REMPI-ReToF-MS represents an elegant tool to overcome the aforementioned limitations with the ultimate goal to identify the carriers of the ion signal at m/z = 93 (C$_6$H$_7$N$^+$) and 117 (C$_8$H$_7$N$^+$). REMPI first accesses an excited state unique to an individual isomer via resonant photon absorption, which is then followed by a second photon absorption to ionize the molecule.[60,64,65] Here, one-color [1 + 1] REMPI schemes were exploited to identify aniline (**4**) and indole (**2**) molecules. To determine their resonant REMPI wavelengths, separate experiments were performed with processed C$_2$H$_2$–NH$_3$ ices. The resonance lines for aniline (**4**) and indole (**2**) were determined experimentally at 293.842 nm (4.219 eV) and 283.817 nm (4.369 eV), respectively (Figures S3 and S4), which correspond to their S$_1$ ← S$_0$ transition origin band. These wavelengths agree well with the literature values of 293.85 nm for aniline[64] and 283.809 ± 0.008 nm for indole.[65] A comparison of the SPI- and REMPI-ReToF-MS TPD profiles at m/z = 93 (C$_6$H$_7$N$^+$) reveals that aniline (**4**) is the major contributor (65 ± 7)% (Figure 4b). The differences between the SPI and REMPI sublimation profiles can be

correlated with the ionization of other C$_6$H$_7$N isomers that cannot be ionized with the [1 + 1] REMPI scheme at a wavelength of 293.842 nm. Also, the one-color [1 + 1] REMPI experiment at a wavelength of 283.817 nm provides evidence for the formation of indole (**2**) (Figure 4d), which represents the largest contributor (75 ± 8)% to the ion signal at m/z = 117 (C$_8$H$_7$N$^+$). A comparison of the TPD profiles extracted by SPI and REMPI reveals that additional C$_8$H$_7$N isomers are formed at lower temperatures (150−225 K), as the TPD profiles of SPI- and REMPI-ReToF-MS measurements only match in the high-temperature range from 180 to 300 K (Figure 4d). In addition, aniline (IE = 7.720 ± 0.002 eV) and indole (IE = 7.7602 ± 0.0006 eV) can be ionized at 7.90 eV. The TPD profiles of m/z = 93 and m/z = 117 recorded at 7.90 eV in irradiated C$_2$H$_2$–NH$_3$ ice match well with that of REMPI measurements measured at 293.842 nm (Figure S5) and 283.817 nm (Figure S6), respectively, further confirming the formation of aniline (**4**) and indole (**2**). A blank experiment was also conducted with acetylene–ammonia ice at 10.49 eV under identical conditions, but without energetic electron processing. No sublimation events were detected at m/z = 67, 93, and 117 (Figure S7), verifying that the formation of indole (**2**), pyrrole (**3**), and aniline (**4**) results from the irradiation exposure of the ices. It is worth noting that REMPI measurements were carried out to search for benzonitrile (C$_7$H$_5$N), quinoline (C$_9$H$_7$N), and 2-cyanonaphthalene (C$_{11}$H$_7$N) in irradiated C$_2$H$_2$–NH$_3$ ices; however, no evidence for their formation was found. Besides the formation of the aforementioned molecules, evidence for the formation of benzene (C$_6$H$_6$, **1**),[47,59] vinylacetylene (C$_4$H$_4$, **5**),[47] ethynylamine (HCCNH$_2$, **6**)[46] and phenylacetylene (C$_8$H$_6$, **7**)[47] in processed acetylene–ammonia ices is provided (Figures S8−S11).

Overall, a combination of SPI-ReToF-MS and REMPI-ReToF-MS provides conclusive evidence on the identification
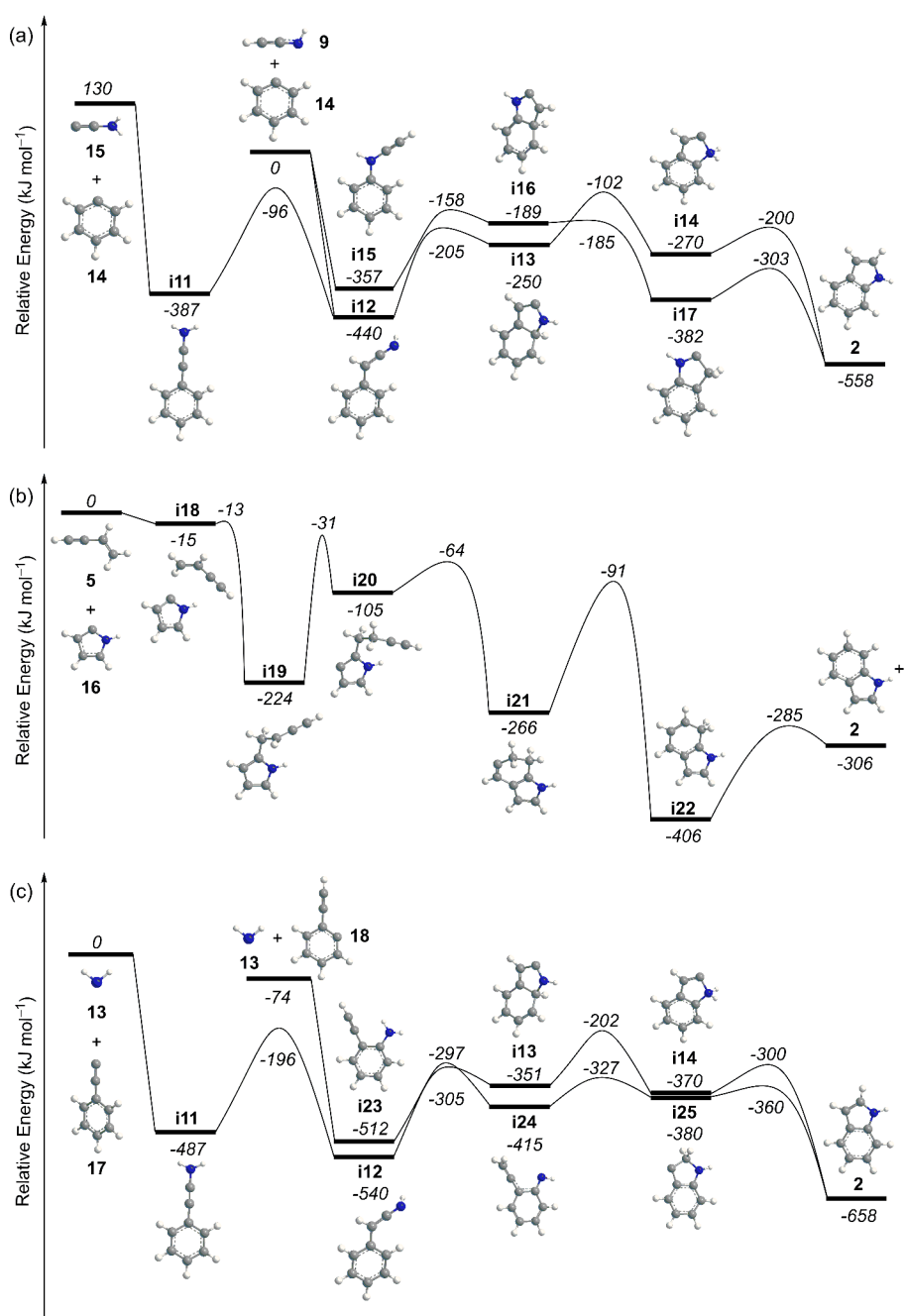
Figure 6. Potential energy surfaces leading to the formation of indole (**2**). Several barrierless pathways are depicted: the reactions of phenyl (C$_6$H$_5$, **14**) radical with aminoethynyl (NH$_2$CC, **15**) radical and ethynylamidogen (HCCNH, **9**) radical (a), the reactions of vinylacetylene (**5**) with 2-pyrrolyl (C$_4$H$_4$N, **16**) radical (b), and the reactions of amino (**13**) radical with phenylethynyl (C$_6$H$_5$CC, **17**) radical and 2-ethynylphenyl (C$_6$H$_4$CCH, **18**) radical (c). The energies (italic) were computed at the G3(MP2,CC)//ωB97X-D/6-311G(d,p) level of theory.

of three nitrogen-containing aromatic molecules in the TPD phase: indole (**2**), pyrrole (**3**), and aniline (**4**).

■ DISCUSSION

With the compelling identification of indole (**2**), pyrrole (**3**), and aniline (**4**), we now turn our attention to potential pathways of their formation (Figure 1) by merging our experimental data with electronic structure calculations predicting the relative energies of all reactants, intermediates, transition states, and products to a precision of 8 kJ mol^{-1} (Figures 5 and 6). These calculations were guided by the development of a retrosynthetic scheme[66−68] deconstructing

indole (**2**), pyrrole (**3**), and aniline (**4**) into fundamental building blocks identified in exposed ammonia−acetylene ices. Aniline (**4**) can be prepared from benzene (**1**)[60] and ammonia; pyrrole (**3**) can be the reaction product from ethynylamine (**6**)[46] and acetylene precursors; five pathways can be identified to prepare indole (**2**): aniline (**4**) plus acetylene, benzene (**1**) plus ethynylamine (**6**), pyrrole (**3**) plus vinylacetylene (**5**),[47] pyrrole (**3**) plus acetylene, and phenylacetylene (**7**)[60] plus ammonia.

Pyrrole (3). Both the ethynylamine (**6**) and acetylene represent closed shell precursors; reactions of two closed shell molecules in their electronic ground states are afflicted by

significant entrance barriers often exceeding 100 kJ mol^{-1}[169] and hence are closed. However, upon exposure to the GCR proxies, ethynylamine (**6**) can undergo unimolecular decomposition via, e.g., hydrogen atom loss from the amino group leading to the ethynylamidogen radical (HCCN$\dot{\text{H}}$, **9**). The suprathermal hydrogen atom can overcome the barrier of 16 kJ mol^{-1}[170] and may add to the carbon–carbon triple bond of acetylene forming the vinyl radical (CH$_2$$\dot{\text{C}}$H, **8**).[47,52,70] Our electronic structure calculation exposed a barrierless reaction of vinyl radical (**8**) and ethynylamidogen radical (**9**) through carbon–carbon coupling and the formation of the acyclic singlet intermediate **i1** (Figure 5a). The latter can isomerize via ring closure to **i2**. Successive hydrogen atom shifts from the CH$_2$ moiety to the nitrogen atom followed by a hydrogen migration from the N–H unit to the carbene carbon atom to form pyrrole (**3**) via intermediates **i2** and **i3**, respectively, in an overall exoergic (−576 kJ mol^{-1}) reaction. Whereas under single collision conditions pyrrole (**3**) undergoes unimolecular decomposition in the gas phase, the surrounding molecules in the ice matrix facilitate a transfer of the internal energy to the neighboring molecules just stabilizing pyrrole (**3**). Instead of adding a hydrogen atom, upon exposure to the GCR proxies, acetylene can also lose atomic hydrogen forming the ethynyl radical (HC$\dot{\text{C}}$, **10**). Our calculations identified two multistep pathways (Figure 5b and 5c) commencing with the ethynyl radical (**10**). In detail, the ethynyl radical (**10**) can add barrierlessly with its radical center to the terminal carbon atom of ethynylamine (**6**) forming the acyclic radical intermediate **i4** (Figure 5b). Trans–cis isomerization to **i5** followed by cyclization to intermediate **i6** and hydrogen shift from the NH$_2$ moiety to the neighboring carbon atom accesses the 3-pyrrolyl radical (**11**). The latter can be reduced through recombination with atomic hydrogen present in the ice yielding pyrrole (**3**). Alternatively, the ethynyl radical (**10**) can react with the 2-aminoethenyl radical (NH$_2$CH$\dot{\text{C}}$H, **12**) through barrierless addition via radical–radical recombination yielding aminovinylacetylene (**i7**) (Figure 5c). The latter isomerizes to intermediate **i8** by the atomic hydrogen transfer from the nitrogen atom to the carbon atom on the opposite end of the molecule, followed by the five-membered ring closure to yield **i9**, which can further form pyrrole (**3**) via hydrogen migration. Overall, our electronic structure calculations identified three barrierless, exoergic routes to the preparation of pyrrole (**3**).

Aniline (4). The retrosynthetic approach guided the synthesis of aniline (**4**) from the benzene (**1**) plus ammonia system. The computations revealed a barrierless recombination of phenyl (**14**) and amino ($\dot{\text{N}}$H$_2$, **13**) radicals accessing aniline (**4**) in a strongly exoergic (−429 kJ mol^{-1}) reaction (Figure 5d). Amino (**13**) and phenyl (**14**) radicals can be formed through GCR induced N–H and C–H bond cleavages of ammonia and benzene.[50] An alternative route (Figure 5e) proceeds through the addition of the amino radical (**13**) to benzene via a barrier of 46 kJ mol^{-1} forming **i10**, which then ejects atomic hydrogen to yield aniline (**4**). Considering the barrierless entrance channel, the reaction of the phenyl radical (**14**) with the amino radical (**13**) likely dominates the formation of aniline (**4**).

Indole (2). Among the five systems identified via retrosynthesis, three systems—benzene (**1**) plus ethynylamine (**6**), pyrrole (**3**) plus vinylacetylene (**5**), phenylacetylene (**7**)[60] plus ammonia—eventually access barrierless pathways (Figure 6). *First*, upon interaction with GCRs, benzene (**1**) and ethynyl-

amine (**6**) can undergo unimolecular decomposition via C–H and/or N–H bond rupture forming the phenyl (**14**) and aminoethynyl (**15**) radicals as well as the phenyl (**14**) and ethynylamidogen (**9**) radicals, respectively. Phenyl (**14**) and aminoethynyl (**15**) recombine barrierlessly to form 2-phenylethynamine (**i11**), which isomerizes through hydrogen shift to **i12** (Figure 6a). The latter can also be accessed via the radical–radical reaction of phenyl (**14**) with ethynylamidogen (**9**), which can also form **i15** in the entrance channel. These intermediates can undergo ring closure to **i13** and **i16**, respectively, followed by hydrogen migration to **i14** and **i17**, which in turn undergo another hydrogen shift to indole (**2**). *Second*, pyrrole (**3**) can undergo unimolecular decomposition via C–H bond rupture forming the 2-pyrrolyl (**16**) radical upon interaction with GCRs. The 2-pyrrolyl (**16**) radical forms a van-der-Waals complex **i18** with vinylacetylene (**5**) (Figure 6b), which eventually isomerizes to intermediate **i19**; the latter starts a complex reaction sequence involving a hydrogen shift to **i20**, ring closure to **i21**, hydrogen migration to **i22**, and atomic hydrogen loss to indole (**2**). *Third*, upon interaction with GCRs, phenylacetylene (**7**) can undergo unimolecular decomposition via C–H bond rupture at the ethynyl and phenyl moieties yielding phenylethynyl (C$_6$H$_5$C$\dot{\text{C}}$, **17**) and 2-ethynylphenyl (C$_6$H$_4$CCH, **18**) radicals, respectively. Amino (**13**) and phenylethynyl (**17**) radicals recombine barrierlessly to 2-phenylethynamine (**i11**), which forms indole (**2**) in an identical reaction sequence as for the reaction of phenyl (**14**) with aminoethynyl (**15**) (Figure 6a and 6c). The radical–radical reaction of amino (**13**) with 2-ethynylphenyl (**18**) prepares 2-aminophenylacetylene (**i23**), which isomerizes through hydrogen shift to **i24**. The latter undergoes ring closure to **i25** followed by hydrogen migration to indole (**2**). Both pathways are barrierless and exoergic by 658 kJ mol^{-1}. Altogether, these routes are barrierless and highly exoergic with the internal energy of indole (**2**) transferrable to the neighboring molecules eventually stabilizing indole (**2**).

■ CONCLUSIONS

The present work demonstrates the first preparation of the astronomically elusive indole (**2**), pyrrole (**3**), and aniline (**4**) in interstellar model ices. This is accomplished in low-temperature acetylene–ammonia ices upon exposure to proxies for GCRs in cold molecular clouds. These nitrogenous heteroaromatics were identified in the gas phase by PI-ReToF-MS along with PIE curves and REMPI techniques during the TPD phase simulating the transition from cold molecular clouds to star forming regions. These experiments demonstrate the implementation of REMPI-ReToF-MS as an isomer-selective detection method to identify nitrogen heteroaromatics with unprecedented sensitivity. Our combined laboratory experimental results and electronic structure calculations reveal plausible formation pathways to these aromatics via GCR-mediated nonequilibrium chemistries operating under astrophysical environments thus providing crucial steps toward a systematic elucidation of the formation mechanisms of interstellar NPAHs, aromatic amino acids, and nucleobases in deep space. Experiments were performed at around 5 K, a temperature that contributes a similar thermal influence on a variety of astrophysical environments, there would not be a significant influence on radical–radical and radical–neutral reactions at higher temperatures such as 10 K. Following the reaction mechanisms elucidated here, indole (**2**), pyrrole (**3**), and aniline (**4**) are likely generated in

interstellar ices after exposure to ionizing sources at doses readily achievable within the lifetimes of molecular clouds of up to 2×10^7 years. Upon the transition from the cold cloud to a star-forming region, these molecules may sublime into the gas phase during the warm-up phase. Considering the large dipole moments of indole (1.96 D),[71] pyrrole (1.74 D),[72] and aniline (1.13 D)[73] along with their known rotational spectra,[72−74] they represent ideal candidates to be searched for in star-forming regions and hot molecular cores via radio telescopes such as the Atacama Large Millimeter/submillimeter Array (ALMA) and the James Webb Space Telescope (JWST).

Once formed on ice-coated interstellar grains by energetic processing in cold molecular clouds, indole (**2**) along with its molecular building blocks pyrrole (**3**) and aniline (**4**) may also act as precursors to key biorelevant molecules. The reaction of pyrrole (**3**) with the methylidyne radical can lead to pyridine,[36] an extra key building block of NPAHs.[21,22] As one of the simplest NPAHs, indole (**2**) can also participate in molecular mass growth processes to form more complex NPAHs and contribute to the formation of nucleobases (Figure 1), which are essential building blocks of the genetic molecules DNA and RNA.[13] In addition, indole (**2**) is a substituent of the proteinogenic amino acid tryptophan. During the formation of solar systems, these molecules can also be incorporated into planetoids, asteroids, and comets, which can carry them into the atmosphere of young planets such as the early Earth.[19] In fact, extraterrestrial NPAHs such as (iso)quinoline and purine nucleobases adenine ($C_5H_5N_5$) and guanine ($C_5H_5N_5O$) and pyrimidine nucleobases cytosine ($C_4H_5N_3O$), uracil ($C_4H_4N_2O_2$), and thymine ($C_5H_6N_2O_2$) were identified in carbonaceous meteorites.[30,75−77] Therefore, those organics could have been delivered to the early Earth as an exogenous source of biorelevant molecules, providing a plausible pathway to the formation of key biomolecules related to the *Origins of Life* on the prebiotic Earth.[78]

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.4c09449.

> Methods and Materials (Experimental and Computational), PI-ReToF-MS data of irradiated acetylene−ammonia ice (Figure S1), TPD profiles of $m/z = 67$ measured at 10.49 and 7.90 eV in irradiated C_2H_2−NH_3 ice (Figure S2), REMPI scans for aniline and indole (Figures S3 and S4), TPD profiles of $m/z = 93$ and 117 measured at 10.49 and 7.90 eV and the REMPI wavelengths in irradiated C_2H_2−NH_3 ice (Figures S5 and S6), TPD profiles for the blank experiment (Figure S7), the formation of benzene, vinylacetylene, ethynyl-amine, and phenylacetylene (Figures S8−S11) and the C_2H_2−HCN ice (Figure S12), other calculated reaction pathways leading to the formation of pyrrole and indole (Figures S13−S25), FTIR absorptions observed in C_2H_2−NH_3 ice (Table S1), parameters for the generation of VUV and UV lights (Table S2), Cartesian coordinates and vibrational frequencies of optimized structures (Table S3) (PDF)

AUTHOR INFORMATION

Corresponding Authors

Alexander M. Mebel − *Department of Chemistry and Biochemistry, Florida International University, Miami, Florida 33199, United States;* orcid.org/0000-0002-7233-3133; Email: mebela@fiu.edu

Ralf I. Kaiser − *W. M. Keck Research Laboratory in Astrochemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States; Department of Chemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States;* orcid.org/0000-0002-7233-7206; Email: ralfk@hawaii.edu

Authors

Jia Wang − *W. M. Keck Research Laboratory in Astrochemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States; Department of Chemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States*

Anatoliy A. Nikolayev − *Samara National Research University, Samara 443086, Russia*

Joshua H. Marks − *W. M. Keck Research Laboratory in Astrochemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States; Department of Chemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States;* orcid.org/0000-0003-0492-2494

Andrew M. Turner − *W. M. Keck Research Laboratory in Astrochemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States; Department of Chemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States*

Sankhabrata Chandra − *W. M. Keck Research Laboratory in Astrochemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States; Department of Chemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States;* orcid.org/0000-0002-7466-6409

N. Fabian Kleimeier − *W. M. Keck Research Laboratory in Astrochemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States; Department of Chemistry, University of Hawaii at Manoa, Honolulu, Hawaii 96822, United States;* orcid.org/0000-0003-1767-897X

Leslie A. Young − *Department of Space Studies, Southwest Research Institute, Boulder, Colorado 80302, United States*

Complete contact information is available at:
https://pubs.acs.org/10.1021/jacs.4c09449

Notes

The authors declare no competing financial interest.

REFERENCES

(1) McKellar, A. Evidence for the molecular origin of some hitherto unidentified interstellar lines. *Publ. Astron. Soc. Pac.* **1940**, *52*, 187.

(2) Rap, D. B.; Schrauwen, J. G. M.; Marimuthu, A. N.; Redlich, B.; Brünken, S. Low-temperature nitrogen-bearing polycyclic aromatic hydrocarbon formation routes validated by infrared spectroscopy. *Nat. Astron.* **2022**, *6*, 1059−1067.

(3) Canta, A.; Öberg, K. I.; Rajappan, M. The Formation of Imines and Nitriles during VUV Photoirradiation of $NH_3:C_2H_x$ Ice Mixtures. *Astrophys. J.* **2023**, *953*, 81.

(4) Marks, J. H.; Wang, J.; Sun, B.-J.; McAnally, M.; Turner, A. M.; Chang, A. H. H.; Kaiser, R. I. Thermal synthesis of carbamic acid and its dimer in interstellar ices: A reservoir of interstellar amino acids. *ACS Cent. Sci.* **2023**, *9*, 2241–2250.

(5) Wang, L.; Jiang, X.; Trabelsi, T.; Wang, G.; Francisco, J. S.; Zeng, X.; Zhou, M. Spectroscopic study of [Mg, H, N, C, O] species: Implications for the astrochemical magnesium chemistry. *J. Am. Chem. Soc.* **2024**, *146*, 4162–4171.

(6) Landera, A.; Mebel, A. M. Low-temperature mechanisms for the formation of substituted azanaphthalenes through consecutive CN and C_2H additions to styrene and n-methylenebenzenamine: A theoretical study. *J. Am. Chem. Soc.* **2013**, *135*, 7251–7263.

(7) Haupa, K. A.; Tarczay, G.; Lee, Y.-P. Hydrogen abstraction/addition tunneling reactions elucidate the interstellar H_2NCHO/HNCO ratio and H_2 formation. *J. Am. Chem. Soc.* **2019**, *141*, 11614–11620.

(8) Xie, M.; Sun, X.; Li, W.; Guan, J.; Liang, Z.; Hu, Y. A facile route for the formation of complex nitrogen-containing prebiotic molecules in the interstellar medium. *J. Phys. Chem. Lett.* **2022**, *13*, 8207–8213.

(9) Perlin, A. L.; Wolff, W.; Oliveira, R. R. Low energy isomers and infrared spectra simulations of C_4H_3N, C_4H_4N, and C_4H_5N and Related Ions. *J. Phys. Chem. A* **2023**, *127*, 2481–2488.

(10) He, L.; Tomaník, L.; Malerz, S.; Trinter, F.; Trippel, S.; Belina, M.; Slavíček, P.; Winter, B.; Küpper, J. Specific versus Nonspecific Solvent Interactions of a Biomolecule in Water. *J. Phys. Chem. Lett.* **2023**, *14*, 10499–10508.

(11) Laneuville, M.; Kameya, M.; Cleaves, H. J. Earth without life: A systems model of a global abiotic nitrogen cycle. *Astrobiology* **2018**, *18*, 897–914.

(12) Oba, Y.; Takano, Y.; Naraoka, H.; Watanabe, N.; Kouchi, A. Nucleobase synthesis in interstellar ices. *Nat. Commun.* **2019**, *10*, 4413.

(13) Parker, D. S. N.; Kaiser, R. I. On the formation of nitrogen-substituted polycyclic aromatic hydrocarbons (NPAHs) in circumstellar and interstellar environments. *Chem. Soc. Rev.* **2017**, *46*, 452–463.

(14) Zhang, C.; Wang, J.; Turner, A. M.; Marks, J. H.; Chandra, S.; Fortenberry, R. C.; Kaiser, R. I. On the Formation of Vinylamine ($C_2H_3NH_2$) in Interstellar Ice Analogs. *Astrophys. J.* **2023**, *952*, 132.

(15) Marks, J. H.; Nikolayev, A. A.; Evseev, M. M.; Wang, J.; Turner, A. M.; Kleimeier, N. F.; Kuznetsov, O. V.; McAnally, M.; Morozov, A. N.; Antonov, I. O.; et al. Quantum-tunneling-mediated synthesis of prebiotic chelation agents in interstellar analog ices. *Chem* **2023**, *9*, 3286–3303.

(16) Stan-Bernhardt, A.; Glinkina, L.; Hulm, A.; Ochsenfeld, C. Exploring chemical space using Ab initio hyperreactor dynamics. *ACS Cent. Sci.* **2024**, *10*, 302–314.

(17) Ehrenfreund, P.; Irvine, W.; Becker, L.; Blank, J.; Brucato, J. R.; Colangeli, L.; Derenne, S.; Despois, D.; Dutrey, A.; Fraaije, H.; et al. Astrophysical and astrochemical insights into the origin of life. *Rep. Prog. Phys.* **2002**, *65*, 1427.

(18) Turner, A. M.; Kaiser, R. I. Exploiting photoionization reflectron time-of-flight mass spectrometry to explore molecular mass growth processes to complex organic molecules in interstellar and solar system ice analogs. *Acc. Chem. Res.* **2020**, *53*, 2791–2805.

(19) Arumainayagam, C. R.; Garrod, R. T.; Boyer, M. C.; Hay, A. K.; Bao, S. T.; Campbell, J. S.; Wang, J.; Nowak, C. M.; Arumainayagam, M. R.; Hodge, P. J. Extraterrestrial prebiotic molecules: Photochemistry vs. radiation chemistry of interstellar ices. *Chem. Soc. Rev.* **2019**, *48*, 2293–2314.

(20) McGuire, B. A. 2021 Census of interstellar, circumstellar, extragalactic, protoplanetary disk, and exoplanetary molecules. *Astrophys. J., Suppl. Ser.* **2022**, *259*, 30.

(21) Marks, J. H.; Wang, J.; Fortenberry, R. C.; Kaiser, R. I. Preparation of methanediamine ($CH_2(NH_2)_2$)—A precursor to

nucleobases in the interstellar medium. *Proc. Natl. Acad. Sci. U.S.A.* **2022**, *119*, No. e2217329119.

(22) McGuire, B. A.; Burkhardt, A. M.; Kalenskii, S.; Shingledecker, C. N.; Remijan, A. J.; Herbst, E.; McCarthy, M. C. Detection of the aromatic molecule benzonitrile (c-C_6H_5CN) in the interstellar medium. *Science* **2018**, *359*, 202–205.

(23) McGuire, B. A.; Loomis, R. A.; Burkhardt, A. M.; Lee, K. L. K.; Shingledecker, C. N.; Charnley, S. B.; Cooke, I. R.; Cordiner, M. A.; Herbst, E.; Kalenskii, S.; et al. Detection of two interstellar polycyclic aromatic hydrocarbons via spectral matched filtering. *Science* **2021**, *371*, 1265–1269.

(24) Sita, M. L.; Changala, P. B.; Xue, C.; Burkhardt, A. M.; Shingledecker, C. N.; Kelvin Lee, K. L.; Loomis, R. A.; Momjian, E.; Siebert, M. A.; Gupta, D.; et al. Discovery of interstellar 2-cyanoindene (2-C_9H_7CN) in GOTHAM observations of TMC-1. *Astrophys. J. Lett.* **2022**, *938*, L12.

(25) Peeters, Z.; Botta, O.; Charnley, S. B.; Ruiterkamp, R.; Ehrenfreund, P. The astrobiology of nucleobases. *Astrophys. J.* **2003**, *593*, L129.

(26) Charnley, S. B.; Kuan, Y.-J.; Huang, H.-C.; Botta, O.; Butner, H. M.; Cox, N.; Despois, D.; Ehrenfreund, P.; Kisiel, Z.; Lee, Y.-Y.; et al. Astronomical searches for nitrogen heterocycles. *Adv. Space Res.* **2005**, *36*, 137–145.

(27) Mebel, A. M.; Landera, A.; Kaiser, R. I. Formation mechanisms of naphthalene and indene: From the interstellar medium to combustion flames. *J. Phys. Chem. A* **2017**, *121*, 901–926.

(28) Ye, H.; Alessandrini, S.; Melosso, M.; Puzzarini, C. Exploiting the "Lego brick" approach to predict accurate molecular structures of PAHs and PANHs. *Phys. Chem. Chem. Phys.* **2022**, *24*, 23254–23264.

(29) Hudgins, D. M.; Bauschlicher, C. W., Jr.; Allamandola, L. J. Variations in the peak position of the 6.2 μm interstellar emission feature: A tracer of N in the interstellar polycyclic aromatic hydrocarbon population. *Astrophys. J.* **2005**, *632*, 316.

(30) Stoks, P. G.; Schwartz, A. W. Basic nitrogen-heterocyclic compounds in the Murchison meteorite. *Geochim. Cosmochim. Acta* **1982**, *46*, 309–315.

(31) Materese, C. K.; Nuevo, M.; Sandford, S. A. N-and O-heterocycles produced from the irradiation of benzene and naphthalene in H_2O/NH_3-containing ices. *Astrophys. J.* **2015**, *800*, 116.

(32) Parker, D. S. N.; Kaiser, R. I.; Kostko, O.; Troy, T. P.; Ahmed, M.; Mebel, A. M.; Tielens, A. G. G. M. Gas phase synthesis of (iso)quinoline and its role in the formation of nucleobases in the interstellar medium. *Astrophys. J.* **2015**, *803*, 53.

(33) Zhao, L.; Prendergast, M.; Kaiser, R. I.; Xu, B.; Lu, W.; Ahmed, M.; Hasan Howlader, A.; Wnuk, S. F.; Korotchenko, A. S.; Evseev, M. M.; et al. A molecular beam and computational study on the barrierless gas phase formation of (iso)quinoline in low temperature extraterrestrial environments. *Phys. Chem. Chem. Phys.* **2021**, *23*, 18495–18505.

(34) Barik, S. The uniqueness of tryptophan in biology: Properties, metabolism, interactions and localization in proteins. *Int. J. Mol. Sci.* **2020**, *21*, 8776.

(35) Rothemund, P. Formation of porphyrins from pyrrole and aldehydes. *J. Am. Chem. Soc.* **1935**, *57*, 2010–2011.

(36) Soorkia, S.; Taatjes, C. A.; Osborn, D. L.; Selby, T. M.; Trevitt, A. J.; Wilson, K. R.; Leone, S. R. Direct detection of pyridine formation by the reaction of CH (CD) with pyrrole: a ring expansion reaction. *Phys. Chem. Chem. Phys.* **2010**, *12*, 8750–8758.

(37) Yeghikyan, A. G. Irradiation of dust in molecular clouds. II. Doses produced by cosmic rays. *Astrophysics* **2011**, *54*, 87–99.

(38) Kaiser, R.; Roessler, K. Theoretical and laboratory studies on the interaction of cosmic-ray particles with interstellar ices. I. Synthesis of polycyclic aromatic hydrocarbons by a cosmic-ray-induced multicenter mechanism. *Astrophys. J.* **1997**, *475*, 144.

(39) Ferrari, B. C.; Slavicinska, K.; Bennett, C. J. Role of suprathermal chemistry on the evolution of carbon oxides and organics within interstellar and cometary ices. *Acc. Chem. Res.* **2021**, *54*, 1067–1079.

(40) Jones, B. M.; Kaiser, R. I. Application of reflectron time-of-flight mass spectroscopy in the analysis of astrophysically relevant ices exposed to ionization radiation: Methane (CH_4) and D4-methane (CD_4) as a case study. *J. Phys. Chem. Lett.* **2013**, *4*, 1965−1971.

(41) Gibb, E. L.; Whittet, D. C. B.; Boogert, A. C. A.; Tielens, A. G. G. M. Interstellar ice: The infrared space observatory legacy. *Astrophys. J., Suppl. Ser.* **2004**, *151*, 35−73.

(42) Furukawa, Y.; Chikaraishi, Y.; Ohkouchi, N.; Ogawa, N. O.; Glavin, D. P.; Dworkin, J. P.; Abe, C.; Nakamura, T. Extraterrestrial ribose and other sugars in primitive meteorites. *Proc. Natl. Acad. Sci. U.S.A.* **2019**, *116*, 24440−24445.

(43) Eckhardt, A. K.; Bergantini, A.; Singh, S. K.; Schreiner, P. R.; Kaiser, R. I. Formation of glyoxylic acid in interstellar ices: A key entry point for prebiotic chemistry. *Angew. Chem., Int. Ed.* **2019**, *58*, 5663−5667.

(44) Chyba, C.; Sagan, C. Endogenous production, exogenous delivery and impact-shock synthesis of organic molecules: an inventory for the origins of life. *Nature* **1992**, *355*, 125−132.

(45) Sandford, S. A.; Nuevo, M.; Bera, P. P.; Lee, T. J. Prebiotic astrochemistry and the formation of molecules of astrobiological interest in interstellar clouds and protostellar disks. *Chem. Rev.* **2020**, *120*, 4616−4659.

(46) Turner, A. M.; Chandra, S.; Fortenberry, R. C.; Kaiser, R. I. A photoionization reflectron time-of-flight mass spectrometric study on the detection of ethynamine ($HCCNH_2$) and 2H-azirine (c-H_2CCHN). *ChemPhysChem* **2021**, *22*, 985−994.

(47) Abplanalp, M. J.; Kaiser, R. I. Implications for extraterrestrial hydrocarbon chemistry: Analysis of acetylene (C_2H_2) and D2-acetylene (C_2D_2) ices exposed to ionizing radiation via ultraviolet−visible spectroscopy, infrared spectroscopy, and reflectron time-of-flight mass spectrometry. *Astrophys. J.* **2020**, *889*, 3.

(48) Kim, Y. S.; Kaiser, R. I. On the formation of amines (RNH_2) and the cyanide anion (CN^-) in electron-irradiated ammonia−hydrocarbon interstellar model ices. *Astrophys. J.* **2011**, *729*, 68.

(49) Bottger, G. L.; Eggers, D. F., Jr. Infrared spectra of crystalline C_2H_2, C_2HD, and C_2D_2. *J. Chem. Phys.* **1964**, *40*, 2010−2017.

(50) Zheng, W.; Jewitt, D.; Osamura, Y.; Kaiser, R. I. Formation of nitrogen and hydrogen-bearing molecules in solid ammonia and implications for solar system and interstellar ices. *Astrophys. J.* **2008**, *674*, 1242.

(51) Socrates, G. *Infrared and Raman Characteristic Group Frequencies: Tables and Charts*, 3rd ed.; John Wiley & Sons, Ltd.: New York, 2004.

(52) Abplanalp, M. J.; Kaiser, R. I. Implications for extraterrestrial hydrocarbon chemistry: Analysis of ethylene (C_2H_4) and D4-ethylene (C_2D_4) ices exposed to ionizing radiation via combined infrared spectroscopy and reflectron time-of-flight mass spectrometry. *Astrophys. J.* **2017**, *836*, 195.

(53) Kim, Y. S.; Kaiser, R. I. An infrared spectroscopic study of amorphous and crystalline ices of vinylacetylene and implications for Saturn's satellite Titan. *Astrophys. J., Suppl. Ser.* **2009**, *181*, 543−547.

(54) Brock, A.; Mina-Camilde, N.; Manzanares, C. Vibrational spectroscopy of C-H bonds of C_2H_4 liquid and C_2H_4 in liquid argon solutions. *J. Phys. Chem.* **1994**, *98*, 4800−4808.

(55) Mellouki, A.; Liévin, J.; Herman, M. The vibrational spectrum of pyrrole (C_4H_5N) and furan (C_4H_4O) in the gas phase. *Chem. Phys.* **2001**, *271*, 239−266.

(56) Milligan, D. E.; Jacox, M. E. Matrix-isolation infrared spectrum of the free radical NH_2. *J. Chem. Phys.* **1965**, *43*, 4487−4493.

(57) Wang, J.; Marks, J. H.; Turner, A. M.; Nikolayev, A. A.; Azyazov, V.; Mebel, A. M.; Kaiser, R. I. Mechanistical study on the formation of hydroxyacetone (CH_3COCH_2OH), methyl acetate (CH_3COOCH_3), and 3-hydroxypropanal ($HCOCH_2CH_2OH$) along with their enol tautomers (prop-1-ene-1,2-diol ($CH_3C(OH)CHOH$), prop-2-ene-1,2-diol ($CH_2C(OH)CH_2OH$), 1-methoxyethen-1-ol ($CH_3OC(OH)CH_2$) and prop-1-ene-1,3-diol ($HOCH_2CHCHOH$)) in interstellar ice analogs. *Phys. Chem. Chem. Phys.* **2023**, *25*, 936−953.

(58) Nna-Mvondo, D.; Anderson, C. M. Infrared spectra, optical constants, and temperature dependences of amorphous and crystalline benzene ices relevant to Titan. *Astrophys. J.* **2022**, *925*, 123.

(59) Kleimeier, N. F.; Liu, Y.; Turner, A. M.; Young, L. A.; Chin, C.-H.; Yang, T.; He, X.; Lo, J.-I.; Cheng, B.-M.; Kaiser, R. I. Excited state photochemically driven surface formation of benzene from acetylene ices on Pluto and in the outer solar system. *Phys. Chem. Chem. Phys.* **2022**, *24*, 1424−1436.

(60) Abplanalp, M. J.; Frigge, R.; Kaiser, R. I. Low-temperature synthesis of polycyclic aromatic hydrocarbons in Titan's surface ices and on airless bodies. *Sci. Adv.* **2019**, *5*, No. eaaw5841.

(61) Linstrom, P. J.; Mallard, W. G. NIST Chemistry webBook, NIST Standard Reference Database Number 69, 2013. http://webbook.nist.gov/.

(62) Zhu, C.; Wang, H.; Medvedkov, I.; Marks, J.; Xu, M.; Yang, J.; Yang, T.; Pan, Y.; Kaiser, R. I. Exploitation of synchrotron radiation photoionization mass spectrometry in the analysis of complex organics in interstellar model ices. *J. Phys. Chem. Lett.* **2022**, *13*, 6875−6882.

(63) Xie, M.; Zhou, Z.; Wang, Z.; Chen, D.; Qi, F. Determination of absolute photoionization cross-sections of nitrogenous compounds. *Int. J. Mass Spectrom.* **2011**, *303*, 137−146.

(64) Streibel, T.; Hafner, K.; Mühlberger, F.; Adam, T.; Zimmermann, R. Resonance-enhanced multiphoton ionization time-of-flight mass spectrometry for detection of nitrogen containing aliphatic and aromatic compounds: Resonance-enhanced multiphoton ionization spectroscopic investigation and on-line analytical application. *Appl. Spectrosc.* **2006**, *60*, 72−79.

(65) Vondrák, T.; Sato, S.-i.; Kimura, K. Cation vibrational spectra of indole and indole−argon van der waals complex. A zero kinetic energy photoelectron study. *J. Phys. Chem. A* **1997**, *101*, 2384−2389.

(66) Holtom, P. D.; Bennett, C. J.; Osamura, Y.; Mason, N. J.; Kaiser, R. I. A combined experimental and theoretical study on the formation of the amino acid glycine (NH_2CH_2COOH) and its isomer ($CH_3NHCOOH$) in extraterrestrial ices. *Astrophys. J.* **2005**, *626*, 940−952.

(67) Morales, S. B.; Bennett, C. J.; Le Picard, S. D.; Canosa, A.; Sims, I. R.; Sun, B. J.; Chen, P. H.; Chang, A. H. H.; Kislov, V. V.; Mebel, A. M.; et al. A crossed molecular beam, low-temperature kinetics, and theoretical investigation of the reaction of the cyano radical (CN) with 1,3-butadiene (C_4H_6). A route to complex nitrogen-bearing molecules in low-temperature extraterrestrial environments. *Astrophys. J.* **2011**, *742*, 26.

(68) Förstel, M.; Bergantini, A.; Maksyutenko, P.; Góbi, S.; Kaiser, R. I. Formation of methylamine and ethylamine in extraterrestrial ices and their role as fundamental building blocks of proteinogenic α-amino acids. *Astrophys. J.* **2017**, *845*, 83.

(69) Zhou, L.; Zheng, W.; Kaiser, R. I.; Landera, A.; Mebel, A. M.; Liang, M.-C.; Yung, Y. L. Cosmic-ray-mediated formation of benzene on the surface of Saturn's moon Titan. *Astrophys. J.* **2010**, *718*, 1243.

(70) Bennett, C. J.; Jamieson, C. S.; Osamura, Y.; Kaiser, R. I. Laboratory studies on the irradiation of methane in interstellar, cometary, and solar system ices. *Astrophys. J.* **2006**, *653*, 792−811.

(71) Kang, C.; Korter, T. M.; Pratt, D. W. Experimental measurement of the induced dipole moment of an isolated molecule in its ground and electronically excited states: Indole and indole−H_2O. *J. Chem. Phys.* **2005**, *122*, 174301.

(72) Nygaard, U.; Nielsen, J. T.; Kirchheiner, J.; Maltesen, G.; Rastrup-Andersen, J.; Sørensen, G. O. Microwave spectra of isotopic pyrroles. Molecular structure, dipole moment, and ^{14}N quadrupole coupling constants of pyrrole. *J. Mol. Struct.* **1969**, *3*, 491−506.

(73) Lister, D. G.; Tyler, J. K.; Høg, J. H.; Larsen, N. W. The microwave spectrum, structure and dipole moment of aniline. *J. Mol. Struct.* **1974**, *23*, 253−264.

(74) Vávra, K.; Luková, K.; Kania, P.; Koucký, J.; Urban, Š. Rotational spectra of indole in the lowest vibrational states. *J. Mol. Spectrosc.* **2019**, *363*, No. 111175.

(75) Oba, Y.; Takano, Y.; Furukawa, Y.; Koga, T.; Glavin, D. P.; Dworkin, J. P.; Naraoka, H. Identifying the wide diversity of

extraterrestrial purine and pyrimidine nucleobases in carbonaceous meteorites. *Nat. Commun.* **2022**, *13*, 2008.

(76) Callahan, M. P.; Smith, K. E.; Cleaves, H. J.; Ruzicka, J.; Stern, J. C.; Glavin, D. P.; House, C. H.; Dworkin, J. P. Carbonaceous meteorites contain a wide range of extraterrestrial nucleobases. *Proc. Natl. Acad. Sci. U.S.A.* **2011**, *108*, 13995−13998.

(77) Sephton, M. A. Organic compounds in carbonaceous meteorites. *Nat. Prod. Rep.* **2002**, *19*, 292−311.

(78) Kleimeier, N. F.; Eckhardt, A. K.; Schreiner, P. R.; Kaiser, R. I. Interstellar formation of biorelevant pyruvic acid (CH$_3$COCOOH). *Chem* **2020**, *6*, 3385−3395.