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GAS PHASE SYNTHESIS OF (ISO)QUINOLINE AND ITS ROLE IN THE FORMATION OF NUCLEOBASES IN THE INTERSTELLAR MEDIUM

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ABSTRACT

Nitrogen-substituted polycyclic aromatic hydrocarbons (NPAHs) have been proposed to play a key role in the astrochemical evolution of the interstellar medium, yet the formation mechanisms of even their simplest prototypes—quinoline and isoquinoline—remain elusive. Here, we reveal a novel concept that under high temperature conditions representing circumstellar envelopes of carbon stars, (iso)quinoline can be synthesized via the reaction of pyridyl radicals with two acetylene molecules. The facile gas phase formation of (iso)quinoline in circumstellar envelopes defines a hitherto elusive reaction class synthesizing aromatic structures with embedded nitrogen atoms that are essential building blocks in contemporary biological-structural motifs. Once ejected from circumstellar shells and incorporated into icy interstellar grains in cold molecular clouds, these NPAHs can be functionalized by photo processing forming nucleobase-type structures as sampled in the Murchison meteorite.

Key words: astrochemistry – ISM: molecules – methods: laboratory: molecular – molecular processes

1. INTRODUCTION

During the last half century, the investigation of the formation of nitrogen-substituted polycyclic aromatic hydrocarbons (NPAHs)—organic molecules carrying fused benzene rings in which one or more carbon–hydrogen (CH) moieties are replaced by nitrogen atoms—has received considerable attention to rationalize the astrochemical evolution of the interstellar medium (ISM; Ehrenfreund & Sephton 2006; Ziurys 2006; Cherchneff 2011; Rollins et al. 2014). This is due to the key role NPAHs play in the prebiotic evolution of the ISM (Ehrenfreund & Sephton 2006) coupled with the recent identification of nucleobases in carbonaceous chondrites such as Lonewolf Nunataks 94102 and Murchison (Sephton 2002; Callahan et al. 2011). Nucleobases are aromatic molecules consisting of monocyclic (pyrimidine) or bicyclic (purine) structures, which are the basic building blocks of the nucleotide subunits of ribonucleic acid. The discovery of terrestrially rare nucleobases 2,6-diaminopurine and 6,8-diaminopurine in these meteorites (Callahan et al. 2011) together with $^{15}N/^{14}N$ and D/H isotope enrichments (Pizzarello & Huang 2005; Pizzarello & Holmes 2009) in the organic matter strongly suggest an interstellar origin. Furthermore, the infrared spectra of almost all objects in space show strong emission bands at 3.3, 6.2, 7.7, 11.2, and 12.7 μm which are generally attributed to ultra violet-pumped infrared fluorescence by a population of polycyclic aromatic hydrocarbons (PAHs) with more than 50 carbon atoms (Tielens 2008). However, the interstellar 6.2 μm band occurs at too short a wavelength compared to matrix isolation studies and computations of these species. One leading explanation for this discrepancy is the presence of nitrogen-substituted PAH structures (Hudgins et al. 2005). Alternatively, protonated PAHs could account for this band (Knorke et al. 2009; Ricks et al. 2009).

Contemporary astrochemical models exploiting complex networks of chemical reactions involving hydrogen cyanide (HCN) speculate that the nucleobase adenine can be synthesized during the collapse of a cold molecular cloud (Chakrabarti & Chakrabarti 2000). Alternatively, a viable pathway to synthesize prebiotic molecules has been proposed to involve the photo processing of interstellar ices at 10 K (Bernstein et al. 1999; Nuevo et al. 2009, 2014). Nevertheless, these pathways are restricted to adding functional groups to the existing aromatic molecules. Recently, adopted from the combustion chemistry community, NPAHs have been suggested to form via gas phase processes similar to the synthesis of PAHs, which involve reactions of neutral molecules, mainly acetylene (C_2H_2), with aromatic radicals like phenyl (C_6H_5) via the Hydrogen-Abstraction-aCetylene Addition (HACA) mechanism (Frenklach & Feigelson 1989; Parker et al. 2014) operating in circumstellar envelopes at temperatures as high as a few thousand K. Considering that nitrogen is the fourth most abundant element is isoelectronic with the CH group in aromatic molecules, the HACA mechanism has been theoretically proposed to lead to (iso)quinoline—the *prototype NPAHs* derived from naphthalene by substituting a CH moiety with a nitrogen atom (Ricca et al. 2001). This can be achieved by formally replacing the phenyl radical reactant (C_6H_5) by a pyridyl radical (C_5H_4N) formed via hydrogen abstraction from pyridine (C_5H_4N). The latter is predicted to be synthesized at high temperatures via the reaction of HCN with two acetylene molecules, which are abundant in circumstellar envelopes of carbon stars (Cherchneff 2011; Landera & Mebel 2013). However, as of now, the formation mechanisms of even the prototypical representatives of NPAHs—*quinoline and its isomer isoquinoline* as detected in the Murchison meteorite (Plows et al. 2003)—remain elusive.

Here, we report the very first synthesis of quinoline and isoquinoline (C_9H_7N)—two prototypes of NPAHs—via the gas phase reaction of the meta-pyridyl radical (C_5H_4N) with two acetylene molecules (C_2H_2) at temperatures representing the inner regions of circumstellar envelopes of evolved carbon

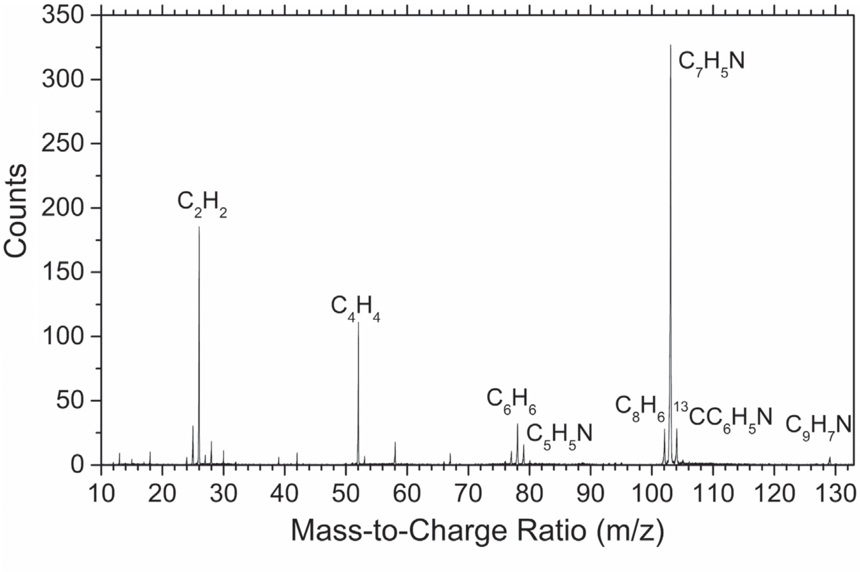

Figure 1. Mass spectrum of the products for the reaction of pyridyl radicals with acetylene in a pyrolytic reactor recorded at a photon energy of 10.0 eV.

stars such as IRC+10216 (Ehrenfreund & Sephton 2006; Cherchneff 2011). In combination with electronic structure calculations, we reveal that the formation of quinoline and its isomer isoquinoline proceeds via a HACA-type mechanism eventually leading to aromatization and formation of (iso) quinoline (C_9H_7N). The facile synthesis of (iso)quinoline and potentially more complex NPAHs in high-temperature circumstellar envelopes represents a hitherto overlooked route to a key class of bio-relevant molecules—NPAHs—in the ISM; it further classifies carbon-rich circumstellar envelopes as "molecular factories" supplying prebiotic molecules to be eventually incorporated into meteors, which can then be further functionalized to nucleobases involving photolysis and possibly aqueous alteration of the parent body (Bernstein et al. 1999; Materese et al. 2013; Nuevo et al. 2014).

2. EXPERIMENTAL

The reaction of the meta-pyridyl radical (C_5H_4N) with two acetylene (C_2H_2) molecules leading to two prototype NPAHs —quinoline and isoquinoline—was studied experimentally in a "pyrolytic reactor," which consists of a resistively heated silicon carbide nozzle, at a temperature of 788 ± 100 K (Kohn et al. 1992). A continuous beam of meta-pyridyl radicals (C_5H_4N) was generated in situ via pyrolysis of the precursor meta-iodopyridine (C_5H_4NI). The latter was seeded in neat acetylene (C_2H_2), which was expanded into a resistively heated silicon carbide tube. The acetylene molecules did not only act as a seeding gas, but also as a reactant with the pyrolytically generated meta-pyridyl radicals. The unique advantage of the experimental setup is the capability to sample the reaction products in situ within the molecular beam after passing the skimmer located downstream from the silicon carbide nozzle. The neutral molecular beam was interrogated by quasi-continuous tunable VUV radiation in the extraction region of a Wiley–McLaren Reflectron Time-of-Flight mass spectrometer. The molecules were single photon ionized and then collected by a microchannel plate detector. A mass spectrum was obtained at intervals of 0.05 eV photon energy between 8.00 and 10.00 eV.

3. THEORETICAL METHODS

Geometries of various species including reactants, intermediates, transition states, and products involved in different reaction mechanisms were optimized at the hybrid density functional B3LYP/6-311G(d,p) level of theory (Stephens et al. 1994). Vibrational frequencies and zero-point vibrational energy (ZPE) were obtained within the same theoretical approach. Single-point energies were refined at the G3(MP2, CC)//B3LYP level of theory, a modification (Baboul et al. 1999; Curtiss et al. 1999) of the original Gaussian 3 method (Frisch et al. 2003). Within the modified theoretical scheme, the final energies at 0 K were obtained according to the following equation.

$$\mathrm{E[G3(MP2,\ CC)] = E[CCSD(T)/6\text{-}311G(d,p)]} \\ + \Delta\mathrm{E(MP2)} + \mathrm{E(ZPE)},$$

where $\Delta E(MP2) = E[MP2/G3Large] – E[MP2/6\text{-}311G(d,p)]$ is the basis set correction and E(ZPE) is the zero-point energy. $\Delta E(SO)$, a spin–orbit correction, and $\Delta E(HLC)$, a higher level correction, from the original G3 scheme were not included, as here they are not expected to make significant contributions to the relative energies. The anticipated accuracy of the G3(MP2, CC)//B3LYP/6-311G(d,p) relative energies is within 10 kJ mol^{-1}. GAUSSIAN 09 (Frisch et al. 2009) and MOLPRO 2010 (Werner et al. 2010) were used for the ab initio calculations.

4. RESULTS

4.1. Experimental Results

Figure 1 depicts a typical mass spectrum recorded at 10.00 eV photoionization energy with product peaks generated via the reaction of the meta-pyridyl radical with acetylene at mass-to-charge ratios of m/z 103 ($C_7H_5N^+$) and m/z 129 ($C_9H_7N^+$). In view of the molecular mass of the reactants of meta-pyridyl (C_5H_4N; 78 u) and acetylene (C_2H_2; 26 u), we determine that the C_7H_5N product (103 u) is formed through addition of acetylene (C_2H_2; 26 u) to meta-pyridyl (C_5H_4N;

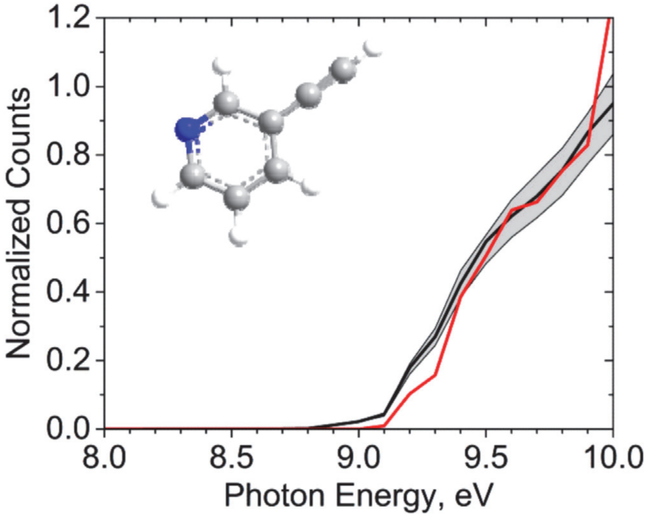

Figure 2. Photoionization energy curve (PIE) recorded at m/z 103 shown as a black line with experimental errors defined as the shaded area. The experimentally determined PIE curve of meta-ethynyl pyridine is shown as the red line.

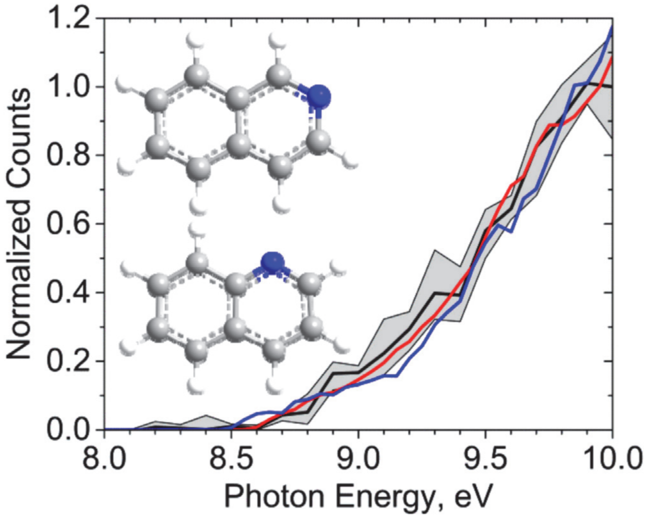

Figure 3. Photoionization energy curve (PIE) recorded at m/z 129 shown as a black line along with experimental errors defined as the shaded area. The experimentally determined PIE curves for quinoline and isoquinoline are shown as the red and blue lines, respectively.

78 u) yielding a C_7H_6N intermediate (104 u), which then emits a hydrogen atom (H; 1 u) to form the product C_7H_5N (103 u). The second product C_9H_7N (129 u) ranges 26 u higher in mass than C_7H_5N (103 u). This mass difference resembles the molecular mass of one acetylene molecule (C_2H_2; 26 u). Therefore, we may propose that the C_9H_7N product (129 u) is formed via reaction of de facto two acetylene molecules (C_2H_2; 26 u) with one meta-pyridyl radical (C_5H_4N; 78 u) accompanied with an atomic hydrogen loss (1 u).

The interpretation of the raw data alone provides convincing evidence that in the reaction of meta-pyridyl radicals with acetylene, two products of the molecular formula C_7H_5N and C_9H_7N are formed. We shift our attention now to the identification of the product isomer(s) formed based on an analysis of the photoionization efficiency (PIE) curves, which report the intensities of the ions at m/z 103 ($C_7H_5N^+$) and m/z 129 ($C_9H_7N^+$) as a function of photon energy (Figures 2 and 3). Here, the experimental data as displayed in black matches the PIE curve of the meta-ethynyl pyridine (C_7H_5N) isomer in red, which was measured separately by seeding meta-ethynyl pyridine (C_7H_5N) in helium carrier gas and recording the PIE curves at m/z 103 ($C_7H_5N^+$; Figure 2). The interpretation of the PIE curve at m/z 129 is more complex. The experimental data can be matched by reference PIEs collected for quinoline and isoquinoline as shown by the red and blue lines respectively. The structural similarities of these m/z 129 isomers (both are aromatic, bicyclic, and contain a single nitrogen atom in the ring) result in indistinguishable PIE curves. The similarity between both PIEs coupled with the experimental error limits does not allow differentiation between these isomers under our experimental conditions. We stress that C_9H_7N isomers other than quinoline and isoquinoline such as phenylpropenitrile and 4-ethenyl benzonitrile, have distinctly different ionization energies (Mallard & Linstrom 1993). Therefore, the corresponding PIEs would have different onsets and efficiencies thus altering their shape compared to the m/z 129 PIE observed here. Recent high-resolution threshold photoionization spectra were taken for quinoline and isoquinoline, finding their I.E's to be 8.61 ± 0.02 eV and 8.53 ± 0.02 eV, respectively, in good agreement with our data (Bouwman et al. 2015). Scaling for photon flux and photoionization cross sections, meta-ethynyl pyridine and quinoline/isoquinoline are formed in yields of $95 \pm 5\%$ and $5 \pm 2\%$, respectively.

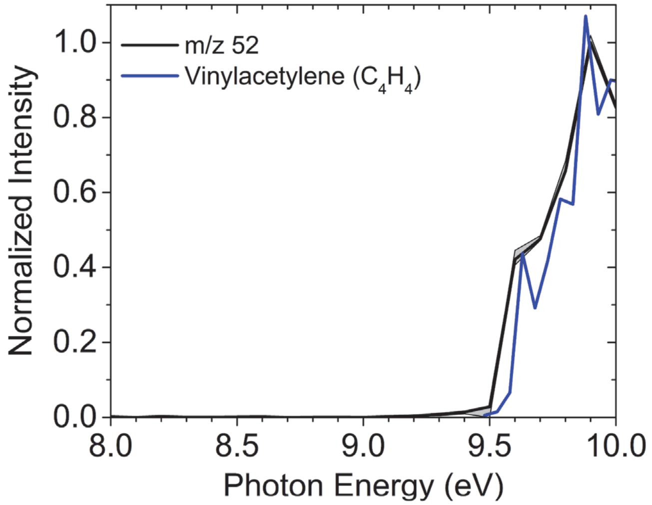

Figure 4. Photoionization efficiency curves recorded at m/z 52 shown as a black line. The blue line shows the experimentally determined reference PIE curve for vinylacetylene (C_4H_4; Cool et al. 2005).

Additional signals can be seen at lower mass-to-charge ratios and can be assigned by matching the corresponding PIE curves to the reference PIEs. Signal at m/z 52, 78, 79, and 102 correspond to vinylacetylene (C_4H_4) (52 u) (Figure 4), benzene (C_6H_6) and fulvene (C_6H_6) (78 u) (Figure 5), pyridine (C_5H_5N) (79 u) (Figure 6), and phenylacetylene (C_8H_6) and benzocyclobutadiene (C_8H_6) (102 u) (Figure 7), respectively. It should be noted that signal at m/z 26 is attributed to acetylene and is visible below its ionization threshold of 11.4 eV. This is because it is the dominant component of the molecular beam, and even though higher harmonics present in the synchrotron beam are effectively removed (<0.0001%), there are still sufficient photons left to ionize acetylene. Pyridine (C_5H_5N) is likely formed via

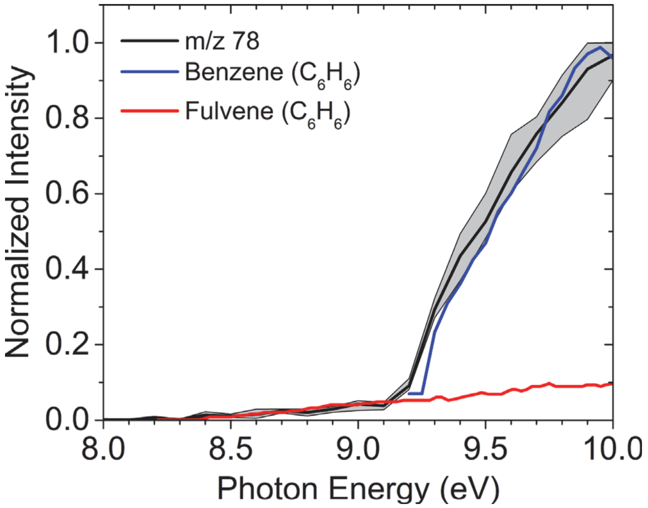

Figure 5. Photoionization efficiency curves (PIE) recorded at m/z 78 shown as a black line. The blue line shows the experimentally determined reference PIE curve for benzene (C_6H_6; Cool et al. 2005) and fulvene (C_6H_6; Soorkia et al. 2010).

hydrogen abstraction by the meta-pyridyl radical from acetylene, which is in excess. Unimolecular decomposition of pyridine can form vinylacetylene (C_4H_4) through HCN elimination (Prather & Lee 1994) or the but-2-yn-1-yl radical (C_4H_5) plus a cyano radical (CN; Lin et al. 2005). Benzene could be synthesized then via the reaction of the C_4H_5 radical plus acetylene (C_2H_2) followed by hydrogen atom elimination (Bittner & Howard 1981; Frenklach 2002); the hydrogen-atom-assisted benzene to fulvene conversion is well established (Madden et al. 1996). Finally, phenylacetylene (C_8H_6) could be formed through the HACA mechanism from benzene (C_6H_6; Parker et al. 2014), which thermally isomerizes to benzocyclobutadiene (C_8H_6; Kuhn et al. 2014).

4.2. *Theoretical Results*

Having identified (iso)quinoline together with meta-ethynyl pyridine as nitrogen-bearing products formed in the reaction of meta-pyridyl radicals with acetylene at elevated temperatures as prevailing in inner regions of circumstellar envelopes of dying carbon stars, we present now the results of complementary electronic structure calculations to propose viable reaction mechanisms. The electronic structure calculations suggest three reaction mechanisms leading to quinoline and isoquinoline formation via two sequential acetylene addition pathways. These pathways resemble the HACA mechanism proposed by Frenklach & Wang (1991) and Bittner & Howard (1981).

Considering the Bittner–Howard related pathway (Figure 8), our calculations suggest that the reaction is initiated by the addition of the meta-pyridyl radical (C_5H_4N) to a single acetylene (C_2H_2) molecule via an entrance barrier of 14 $\mathrm{kJ\ mol^{-1}}$ to form a C_7H_6N collision complex [1], which is stabilized by 166 $\mathrm{kJ\ mol^{-1}}$ with respect to the separated reactants. The meta-ethynyl pyridine product (C_7H_5N) can be formed by isomerization of [1] over a small barrier of only 9 $\mathrm{kJ\ mol^{-1}}$ to [2] through rotation of the acetylene moiety followed by a hydrogen atom elimination from the acetylenic carbon atom over an exit barrier of 28 $\mathrm{kJ\ mol^{-1}}$ in an overall exoergic reaction (−40 $\mathrm{kJ\ mol^{-1}}$) as shown in Figure 9. Our computations also portray two routes leading to characteristic four carbon atom chain structures of intermediates [9]/[10] that precede cyclization. The lowest energy route to [9] and [10] involves *trans* to *cis* isomerization of [1]/[2] yielding [3]/[4]. Acetylene addition to [3]/[4] is achieved over small barriers of only 24 $\mathrm{kJ\ mol^{-1}}$, which are well below the total energy of the separated reactants, to reach intermediates [9]/[10]. The latter undergo ring closure to intermediates [11]/[12]. Hydrogen elimination from the bridging carbon atoms yields quinoline and isoquinoline with overall exoergicities of 437 and 432 $\mathrm{kJ\ mol^{-1}}$, respectively. A higher-energy pathway to quinoline and isoquinoline involves acetylene addition to [1]/[2] to reach [5]/[6] followed by rotation of the C4 carbon chain to [7]/[8]; significant energy barriers of 207 and 301 $\mathrm{kJ\ mol^{-1}}$ must be surmounted to form intermediates [9]/[10], respectively. These barriers suggest that reaction pathways involving intermediates

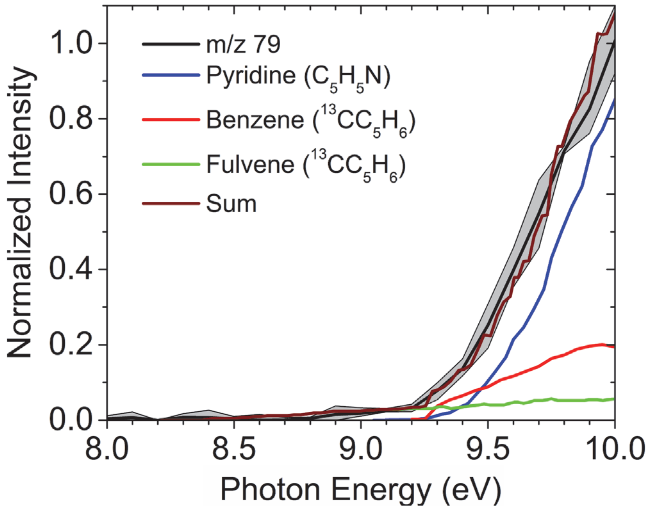

Figure 6. Photoionization efficiency curves recorded at m/z 79 shown as a black line. The dark red line shows the contributions to the signal from experimentally determined reference PIE reference curves for pyridine (C_5H_5N; blue line; Xie et al. 2011), benzene ($^{13}CC_5H_6$; Cool et al. 2005; red line) and fulvene ($^{13}CC_5H_6$; green line; Soorkia et al. 2010).

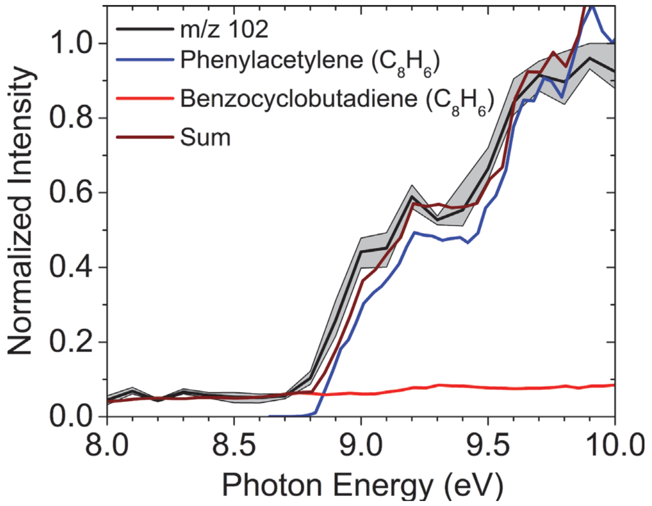

Figure 7. Photoionization efficiency curves recorded at m/z 102 shown as a black line. The dark red line shows the contributions to the signal from experimentally determined reference PIE reference curves for phenylacetylene (C_8H_6; blue line; Zhou et al. 2009) and benzocyclobutadiene (C_8H_6; red line; Li 2011).

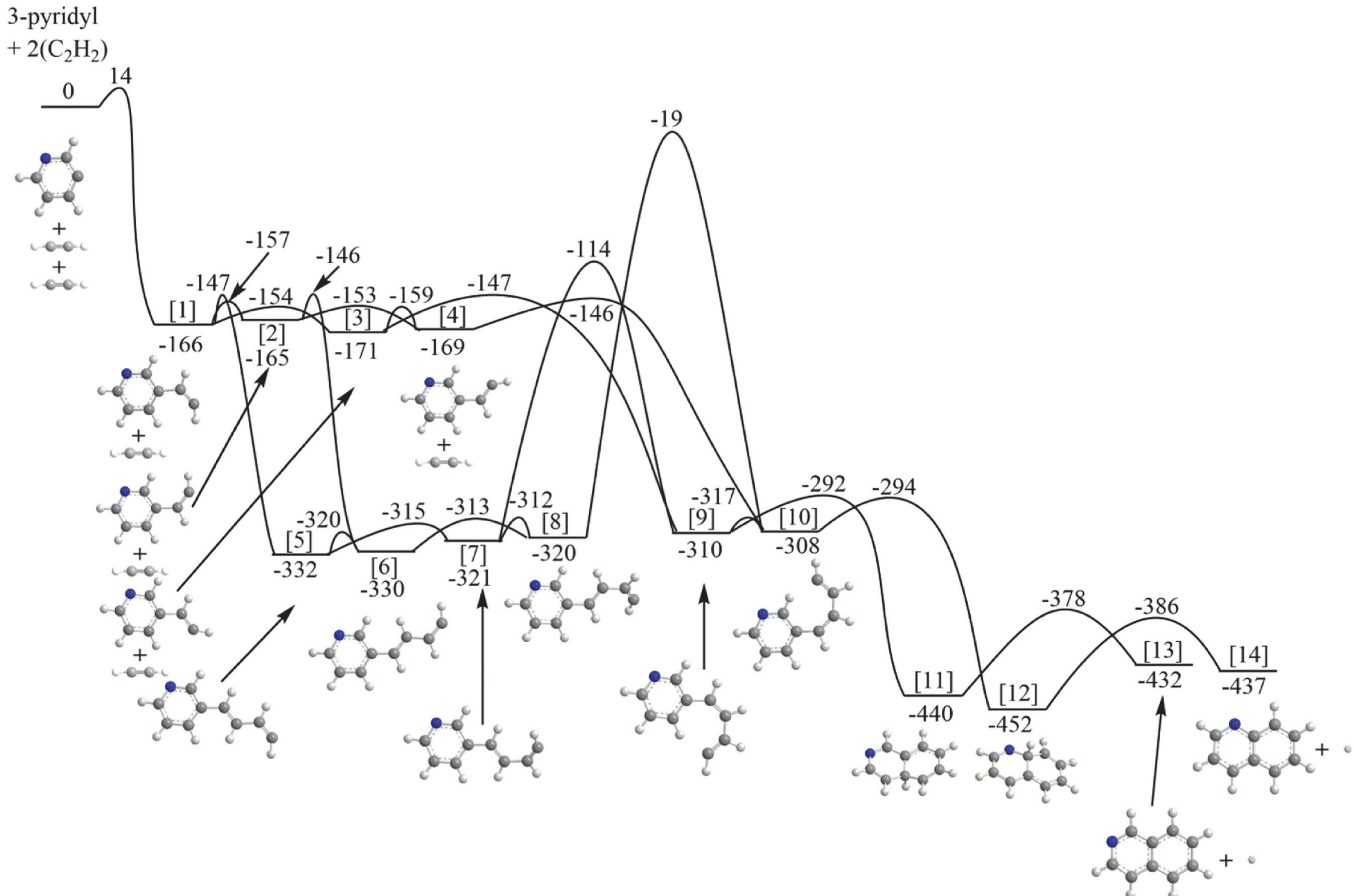

Figure 8. Potential energy surface for the Bittner–Howard HACA mechanism in the reaction of 3-pyridyl radical plus two acetylene molecules. Energy is relative to the reactants and measured in kJ mol^{-1}.

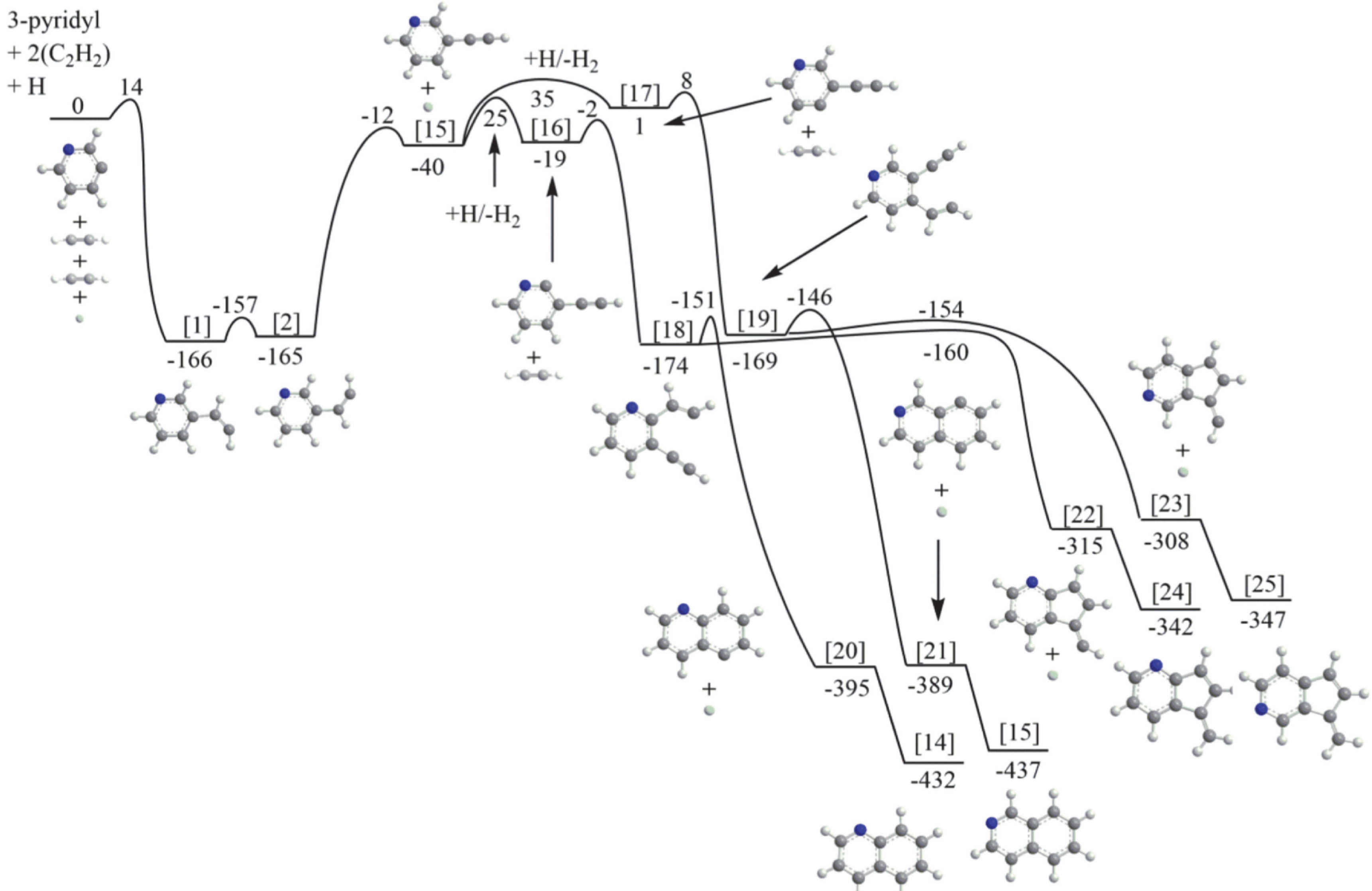

Figure 9. Potential energy surface for the Frenklach HACA mechanism in the reaction of 3-pyridyl radical plus two acetylene molecules and one hydrogen atom. Energy is relative to the reactants and measured in kJ mol^{-1}.

[5] to [8] are less favorable compared to the mechanisms proceeding via intermediates [1]–[4].

The Frenklach mechanism (Figure 9) reaches quinoline and isoquinoline after forming meta-ethynyl pyridine plus atomic hydrogen [15]. A hydrogen abstraction by atomic hydrogen from meta-ethynyl pyridine forms [16] and/or [17]. Here, the barrier associated with hydrogen abstraction to [16] is lower in energy by 10 kJ mol^{-1} compared to forming [17]. The C_7H_4N isomers [16] and [17] add a second acetylene molecule to form [18] and [19], respectively. Cyclization stabilizes the complex by about 220 kJ mol^{-1} to yield isomers [20] and [21]. The formation of quinoline and isoquinoline is achieved through hydrogen atom addition to the radical, which is barrierless yielding the C_9H_7N products quinoline and isoquinoline. A route less favorable by 92 kJ mol^{-1} exists to aza-benzofulvenes [24] and [25] via cyclization of [18] and [19] to form a five-membered ring intermediate [22] and [23] followed by a subsequent barrierless hydrogen addition.

Finally, the modified Bittner–Howard mechanism (Figure 10) proceeds via isomerization of intermediates [1]/[2] to [3]/[4] by *trans–cis* isomerization followed by three distinct routes to the central reaction intermediates [28]/[29]. The lowest energy path involves a hydrogen addition to the acetylene group to form [26]/[27] followed by hydrogen abstraction from the aromatic ring to yield [28]/[29]. The highest energy route involves a hydrogen migration from the aromatic ring to the terminal carbon atom of acetylene to yield a vinyl group [28]/[29] over significant energy barriers of 106 and 119 kJ mol^{-1}. A second acetylene addition to [28]/[29] forms [30]/[31]; cyclization of the acetylene group with the vinyl group leads to [32]/[33], which then emit hydrogen atoms to form quinoline and isoquinoline, respectively. Alternatively, [30]/[31] can isomerize to [34]/[35] through rotation of the vinyl group and then undergo a five-membered ring closure to bicyclic intermediates [36]/[37] containing an extra hydrogen adjacent to the CH_2 group; the extra hydrogen atom is then emitted to form the aza-benzofulvenes [24]/[25]. Once again, formation of these isomers is thermodynamically less favorable by 92 kJ mol^{-1} compared to the formation of quinoline and isoquinoline.

5. REACTION MECHANISM

With the experimental identification of meta-ethynyl pyridine (C_5H_4NCCH) and (iso)quinoline (C_9H_7N) together with the theoretical prediction of feasible reaction pathways to form quinoline and isoquinoline at elevated temperatures representative of inner regions of circumstellar envelopes of evolved carbon stars such as IRC +10216, we merge our experimental and computational results in an attempt to propose the predominant reaction mechanism(s). *First*, the reaction of the meta-pyridyl radical (C_5H_4N) with acetylene (C_2H_2) leads to the formation of meta-ethynyl pyridine (C_5H_4NCCH) plus atomic hydrogen, in an overall exoergic reaction (−40 kJ mol^{-1}). The reaction proceeds via the formation of a C_7H_6N complex and is initiated by the addition of the meta-pyridyl radical to the acetylenic carbon atom via a barrier of 14 kJ mol^{-1} (Figure 4). *Second*, we focus on the formation of (iso)quinoline (C_9H_7N). The experimental and computational investigations propose the dominance of the Bittner–Howard reaction mechanism (Figure 4), in which the initial C_7H_6N collision complex [1] of the meta-pyridyl radical (C_5H_4N)—acetylene (C_2H_2) reaction isomerizes to [2]; the doublet radical intermediates [1] and [2] can react with another acetylene molecule to form two doublet C_9H_8N intermediates [9] and [10]. These intermediates undergo ring closure to [11] and [12] followed by hydrogen atom loss and aromatization leading to isoquinoline and quinoline, respectively, in overall strongly exoergic reactions (−432 and −437 kJ mol^{-1}).

The alternative Frenklach reaction mechanism (Figure 10) likely terminates with the formation of meta-ethynyl pyridine (C_5H_4NCCH). If a hydrogen abstraction from meta-ethynyl pyridine does occur, this hydrogen abstraction would not be limited to hydrogen atoms at the C1 and C3 carbon atoms adjacent to the ethynyl group, but should also occur at the hydrogen atom connected to the C4 and C5 carbon atoms of the ring. This would lead to four doublet radicals, which then can react with a second acetylene molecule. It is important to stress that the addition of acetylene to the C1 and C3 radical center leading to [18] and [19] is a prerequisite for cyclization to occur in a later stage of the reaction. However, the reaction intermediates formed by addition of an acetylene molecule to the C4 and C5 radical center cannot undergo ring closure, but would decompose via elimination of a hydrogen atom to di-ethynyl-substituted pyridine products (C_9H_5N; 127 u). These products, however, were clearly not observed in the present experiments. In addition, the Frenklach mechanism suggests the formation of aza-benzofulvenes [24] and [25], which were not observed in the present study. Therefore, a Frenklach-type reaction mechanism leading to (iso)quinoline can be likely ruled out. The lack of observation of any aza-benzofulvenes [24] and [25] products also eliminates the modified Bittner–Howard mechanism. Although a hydrogen assisted isomerization might convert aza-benzofulvenes [24] and [25] to (iso)quinoline, the simultaneous observation of the benzene–fulvene isomer pair, which holds a similar difference in thermodynamical stability of 95 kJ mol^{-1} compared to 141 kJ mol^{-1} in aza-benzofulvenes—(iso)quinoline, predicts that at least a fraction of the aza-benzofulvenes would survive, if formed by any hydrogen-assisted isomerization. The lack of observation of any aza-benzofulvenes strongly suggests that the Frenklach and modified Bittner–Howard mechanisms play a less important role in the formation of (iso)quinoline, and that the latter is predominantly synthesized via a Bittner–Howard mechanism as rationalized above.

6. ASTROPHYSICAL IMPLICATIONS

The facile route to (iso)quinoline (C_9H_7N) formation—*the NPAH prototypes*—together with the detection of meta-ethynyl pyridine (C_5H_4NCCH) provides novel and compelling evidence that (iso)quinoline can be synthesized in the gas phase at elevated temperatures of 788 K via the reaction of the meta-pyridyl radical with two acetylene molecules through a HACA-type reaction mechanism. We discuss now, our results in the context of interstellar environments. *First*, it is important to stress that the addition of the first acetylene molecule to the meta-pyridyl radical must overcome an entrance barrier of 14 kJ mol^{-1} (Figure 4). This alone strongly indicates that the proposed reaction sequence cannot be initiated in cold molecular clouds such as in the TMC-1, where average temperatures of about 10 K would block this reaction since the entrance barrier to addition cannot be overcome. On the other hand, the elevated temperature of a few thousand K in the inner regions of circumstellar envelopes of dying carbon stars like IRC+10216 supplies the required excess energy and allows the reaction to overcome the barrier to addition (Cherchneff 2011).

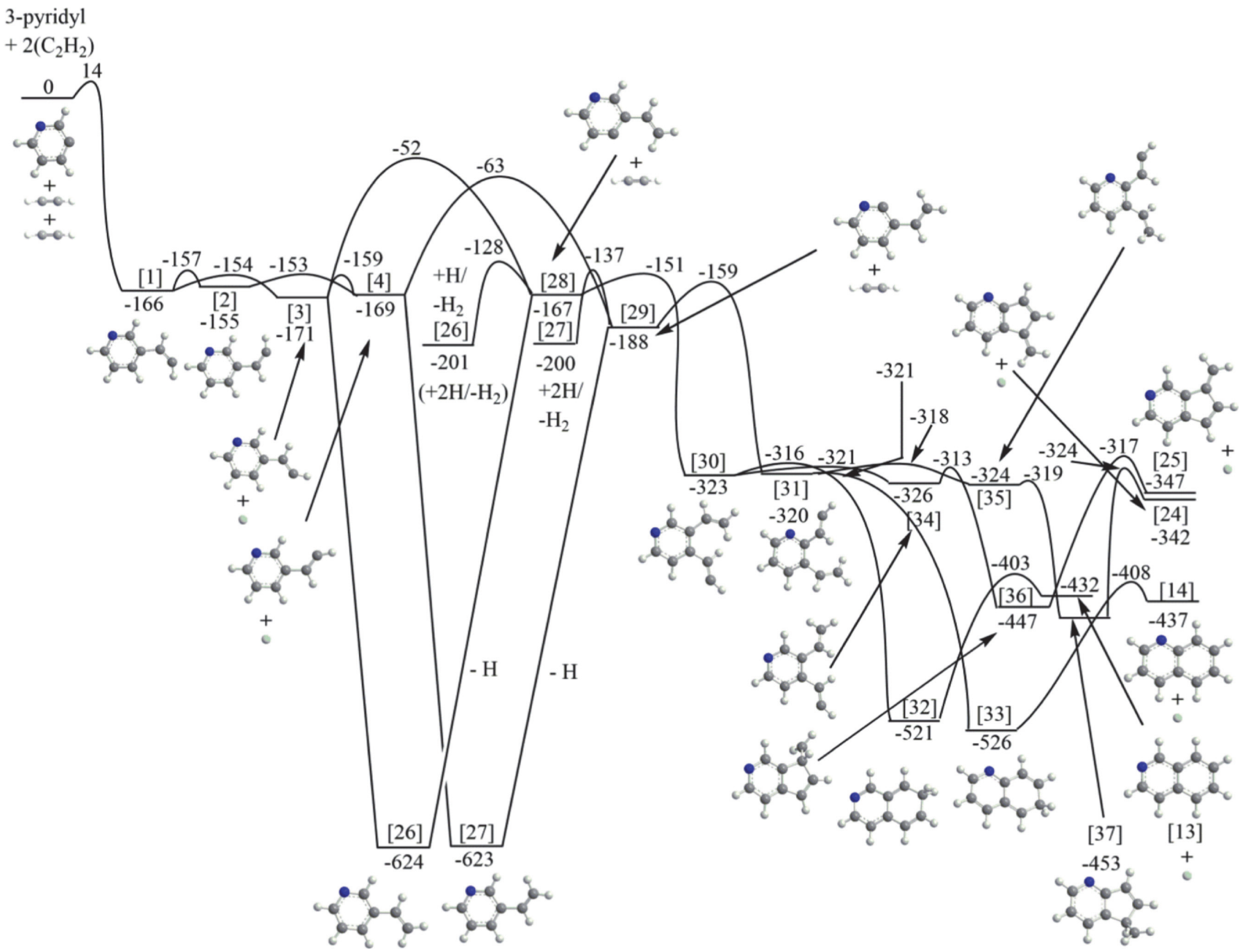

Figure 10. Potential energy surface for the modified Bittner–Howard HACA mechanism in the reaction of 3-pyridyl radical plus two acetylene molecules. Energy is relative to the reactants and measured in kJ mol^{-1}.

The high temperatures in the inner envelopes facilitate a rapid radical-mediated organic chemistry leading to the formation of polycyclic aromatic structures (Tielens et al. 2000; Kislov et al. 2005; Tielens 2008; Cherchneff 2011). *Second*, in addition to establishing that the inner regions of circumstellar envelopes can supply the excess energy necessary to drive the addition of the acetylene to the meta-pyridyl radical and hence initiating the HACA sequence eventually leading to (iso) quinoline (*energy requirement*), we also have to fulfill the prerequisite that the reactants have to be readily available (*chemical requirement*). Here, the HACA mechanism has been implicated to be one of the crucial routes to PAH formation in carbon-rich circumstellar envelopes such as in IRC+10216 considering that acetylene (C_2H_2) is ubiquitous and aromatic radical reactants like phenyl (C_6H_5) and pyridyl (C_5H_4N) are expected to be prevalent (Frenklach & Feigelson 1989; Kislov et al. 2005; Parker et al. 2014). We anticipate that pyridyl radicals form through pyridine (C_5H_5N) via comparable mechanisms that yield phenyl radicals (Zhang et al. 2010) and are likely present considering the large array of nitriles such as vinylcyanide (C_2H_3CN; Agundez et al. 2008) and cyanoacetylene (HCCCN; Jewell & Snyder 1982) detected in these circumstellar envelopes. *Third*, once NPAHs are formed in circumstellar envelopes and eventually incorporated into (icy) interstellar grains in cold molecular clouds, simple NPAHs can be functionalized via non-equilibrium chemistry (Maity et al. 2014) eventually forming nucleobase-type structures such as purines as detected in the Murchison meteorite at levels of up to 0.5 ppm, i.e., about a factor of 30 lower than aromatic compounds probed in Murchison (Callahan et al. 2011). Here, the importance of gas phase chemistry in nucleobase formation is that it provides a chemical starting point to initiate the formation of the aromatic molecular skeleton with the nitrogen(s) incorporated within the aromatic system. Recently, PAHs such as naphthalene ($C_{10}H_8$) have also been shown to be synthesized without entrance barriers via phenyl-type radical-mediated neutral–neutral reactions of, for example, phenyl radicals (C_6H_5) with vinylacetylene (C_4H_4) at ultra-low temperatures in cold molecular clouds at 10 K (Kaiser et al. 2012; Parker et al. 2012). The existence of analogous reaction mechanisms forming NPAHs via the reaction of pyridine radicals (C_5H_4N), which are isoelectronic to phenyl radicals (C_6H_5), with vinylacetylene (C_4H_4) leading to (iso) quinoline and potentially more complex NPAHs is unexplored; dedicated laboratory experiments are warranted to study possible formation routes of these and related species via barrier-less neutral–neutral reactions in cold molecular clouds. Therefore, the gas phase formation of NPAHs (*synthesis of the aromatic structure*) provides a unique link to the subsequent chemical processing of NPAHs in the condensed icy phase (*functionalization of the aromatic structure*) eventually providing a key stage in the formation of prebiotic molecules like nucleobases in the ISM. *Fourth*, the reaction sequence demonstrated in the present study is versatile and can lead via further HACA steps on (iso)quinoline to an efficient growth of large NPAH molecules. In this respect, we would like to recall that that the measured peak position of the interstellar 6.2 μm band can be explained in the context of NPAHs if the nitrogen atom is embedded in the carbon skeleton (Hudgins et al. 2005); this implies pyridine or quinoline as starting compounds. We note that several explanations have been put forward for the "blueshift" of the interstellar 6.2 μm band (Tielens 2013). This study demonstrates that there are efficient routes from pyridine to large NPAHs in the warm, dense stellar ejecta of asymptotic giant branch (AGB) stars.

A recent study of the photostability of NPAHs suggests that once formed, NPAHs might be, to a certain extent, photo destructed by intense ultraviolet radiation (Peeters et al. 2005). Therefore, the "real" NPAH population such as of (iso) quinoline represents the result of the overall formation plus the photo destruction. Consequently, the NPAH population is expected to be low and exist in areas guarded from the ultraviolet radiation field like the inner envelopes of carbon stars where most of the dust is formed (Charnley et al. 2005). As of today, the rationale for NPAH formation in circumstellar envelopes has led to several astronomical searches for pyridine, pyrimidine, quinoline, and isoquinoline toward Sgr B2(N), Orion KL and W51 e1/e2, IRC+ 10219, CRL 618, and CRL 2688 exploiting telescopes such as Arizona Radio Observatory (KP12M), Institute for Radio Astronomy in the Millimeter Range(IRAM 30 m), and Green Bank Telescope (GBT) and comparing these submillimeter range observations to laboratory generated data (Kuan et al. 2003; Charnley et al. 2005). However, no positive assignments have been made yet, most likely due to the expected low population of NPAHs combined with the relatively limited sensitivity of the above mentioned telescopes. Specifically, the upper limit on the column density of pyridine and quinoline in the post-AGB object GL 618 is about $3 \times 10^{13}\,\mathrm{cm}^{-2}$ for an adopted temperature of 200 K, which can be compared to the column density of $5 \times 10^{15}\,\mathrm{cm}^{-2}$ for benzene measured in the mid infrared for this source (Cernicharo et al. 2001). In any case, the explicit identification of (iso)quinoline together with their alkyl-substituted counterparts (Stoks & Schwartz 1982) in Murchison and Lonewolf Nunataks 94102 meteorites combined with their $^{15}N/^{14}N$ and D/H enrichment points to an interstellar heritage, demonstrating that a fraction of the NPAHs—once synthesized in the circumstellar envelopes—survives subsequent photo destruction. Therefore, the search for (iso)quinoline in circumstellar envelopes of carbon-rich stars presents a unique challenge for the recently commissioned Atacama Large Millimeter/Submillimeter Array.

7. CONCLUSION

In summary, our combined experimental and computational study provides compelling evidence and manifests a hitherto overlooked gas-phase synthetic route leading to the formation of a key class of biorelevant molecules in the inner regions of circumstellar envelopes of carbon stars—NPAHs with quinoline and isoquinoline being their prototypical representatives. Once synthesized in the circumstellar envelopes and eventually incorporated into interstellar grains in cold molecular clouds, NPAHs can be functionalized leading to nucleobase-type structures like purines as sampled in the Murchison meteorite. This scenario provides a strong alternative to the terrestrial in situ formation of NPAHs and their functionalized counterparts such as nucleobases on early earth, which have been proposed to involve solutions of hydrogen cyanide (HCN) and ammonia (NH_3; Oro 1961; Roy et al. 2007), condensation—dehydration sequences encompassing formamide ($HCONH_2$; Hudson et al. 2012), and possibly spark discharge of methane (CH_4)—nitrogen (N_2) in the presence of water ice (Menor-Salván et al. 2009; Menor-Salván & Marín-Yaseli 2013).

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