Radical formation of amino acid precursors in interstellar regions? Ser, Cys and Asp†

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Received 9th June 2010, Accepted 19th July 2010
DOI: 10.1039/c0ob00232a

It is proposed that the glycine precursor NH_2CH_2CN may be synthesised in interstellar dust clouds by the radical combination reactions $NH_2^{\bullet} + {}^{\bullet}CH_2CN \rightarrow NH_2CH_2CN$ ($\Delta G = -302$ kJ mol^{-1}) and/or $NH_2CH_2^{\bullet} + {}^{\bullet}CN \rightarrow NH_2CH_2CN$ ($\Delta G = -414$ kJ mol^{-1}). All calculations at the CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory. This paper extends that concept to radical/radical coupling reactions to form Ser, Cys and Asp precursor nitriles. The hydrogen abstraction process $NH_2CH_2CN + HO^{\bullet} \rightarrow NH_2^{\bullet}CHCN + H_2O$ ($\Delta G = -130$ kJ mol^{-1}) is suggested to precede the radical coupling reactions $NH_2^{\bullet}CHCN + R^{\bullet} \rightarrow NH_2CHRCN$ ($R^{\bullet} = {}^{\bullet}CH_2OH$, ${}^{\bullet}CH_2SH$ and ${}^{\bullet}CH_2CN$) to form nitrile precursors of the amino acids Ser, Cys and Asp. These three reactions are all favourable ($\Delta G = -240$, -227 and -223 kJ mol^{-1}). The radical species ${}^{\bullet}CH_2NH_2$, ${}^{\bullet}CH_2OH$, ${}^{\bullet}CH_2SH$ and ${}^{\bullet}CH_2CN$ are shown to be stable for the microsecond timeframe by a combination of theoretical calculations and the experimental mass spectrometric neutralization/reionization procedure.

Introduction

The question as to whether amino acids originated from outer space and/or by chemical reactions on prebiotic Earth is still a matter of debate.[1–3]

Amino acids have been found in meteorites *e.g.*[4–8] and they have also been found following electrical discharge in systems modelling the atmosphere of primordial Earth, *e.g.*[9,10] and following UV irradiation of interstellar ice models.[11,12] The search for the simplest amino acid, glycine, in interstellar dust clouds, circumstellar envelopes, interstellar ice and comets has been ongoing for more than two decades with mixed initial success.[13–21] Perhaps the identification of interstellar glycine has been made difficult because it is likely that amino acids are destroyed by UV photolysis and/or cosmic rays in interstellar clouds.[22,23] In spite of this, the detection of glycine (using rotational spectroscopy) has recently been claimed in the hot molecular cores Sagittarius B2, Orion KL and W5,[24,25] but these reports have been challenged.[26] To date, some 140 molecules have been detected in stellar regions;[22,27–29] suggesting that interstellar molecules could have played an important role of the prebiotic chemistry of Earth.

It has been proposed that amino acids in some meteorites[30] and also in interstellar clouds[31,32] may be formed by the Strecker reaction [$CH_2O + NH_3 + HCN \rightarrow NH_2CH_2CN + H_2O \rightarrow NH_2CH_2CO_2H$[33] ($CH_2O$, NH_3 and HCN are all found in interstellar regions)], or the Tiemann (cyanhydrin) modification of the Strecker process. Other proposals of synthetic routes to glycine in interstellar regions are numerous. Apart from the Strecker reaction, other proposals are that glycine may be formed from formic acid[22,34–37] (particularly in interstellar ice) by reaction with CH_2NH,[34] $CH_3NH_2^{+}$[35] or NH_2CH_2OH[22,37] (*e.g.* $NH_2CH_2OH_2^{+} + HCO_2H \rightarrow NH_2CH_2CO_2H_2^{+} + H_2O$), and from the reaction between acetic acid and $^{+}NH_2OH$.[38] However, utilisation of amines as building blocks for interstellar amino acids has recently been questioned.[39] In addition, it has been shown that the reactions between CH_2NH^{+} and the interstellar molecules HCN or HNC are energetically unfavourable.[40] A recent suggestion is that glycine may be formed in interstellar ice by the multistep process ${}^{\bullet}CH_2NH_2 + CO_2 + H \rightarrow NH_2CH_2CO_2H$.[41]

Two proposals that are particularly interesting in the context of this paper are (i), glycine may be formed by radical coupling reactions (on dust particles or in interstellar ice),[42] and (ii), NH_2CH_2CN may be the precursor of interstellar glycine *cf.*[33] but formed from cyanogen[43] (NCCN, a species not yet detected in interstellar regions) rather than the Strecker process, or by a radical coupling reaction between $NH_2^{\bullet}$ and ${}^{\bullet}CH_2CN$ in a strongly exothermic process.[44]

The proposal of NH_2CH_2CN as a glycine precursor is plausible on several grounds:- namely, (i) amino acids are much less stable to UV irradiation and cosmic rays in interstellar regions than nitriles[22] (which are found throughout interstellar regions,[26,27] including NH_2CH_2CN[28]), and (ii) nitriles should be readily hydrolysed to carboxylic acids in interstellar ice in exothermic reactions with only small barriers (barrier calculated ca 6 kJ mol^{-1} [40]).

In this paper, we investigate the formation of precursors of Ser, Cys and Asp by radical coupling reactions. Cognate ionic reactions may also be possibilities: they have not been considered in this study.

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† Electronic supplementary information (ESI) available: Table S1. Energy and geometry of minima and transitions state for the interconversion of $NH_2CH_2^{\bullet}$ and $CH_3NH^{\bullet}$; Table S2. Energy and geometry data of minima and transition state for the reaction between NH_2CH_2CN and $HO^{\bullet}$; Table S3. Energy and geometry data of minima and transition state for the interconversion of ${}^{\bullet}CH_2SH$ and $CH_3S^{\bullet}$; Table S4. Energy and geometry data of minima and transition states for the interconversion of ${}^{\bullet}CH_2CN$ and ${}^{\bullet}CH_2NC$. See DOI: 10.1039/c0ob00232a

Results and discussion

1. The formation of NH_2CH_2CN

In a previous study it was proposed that aminoacetonitrile could be formed by a radical coupling reaction between the interstellar radicals $^{\bullet}NH_2$ and $^{\bullet}CH_2CN$ as shown in eqn (1), a process favourable by 302 kJ mol^{-1} (at the CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory). All energies indicated in the text are ΔG values calculated at 298 K.

$$^{\bullet}NH_2 + {}^{\bullet}CH_2CN \rightarrow NH_2CH_2CN\ (-302\ \text{kJ mol}^{-1}) \quad (1)$$

$$NH_2CH_2^{\bullet} + {}^{\bullet}CN \rightarrow NH_2CH_2CN\ (-414\ \text{kJ mol}^{-1}) \quad (2)$$

Another possible synthesis is the barrierless reaction shown in eqn (2), a reaction favourable by 414 kJ mol^{-1}. The cyanide radical is a known interstellar molecule, whereas $NH_2CH_2^{\bullet}$ has not, as yet, been identified in interstellar molecular clouds.[29] However, methylamine is an interstellar molecule,[29] and it has been proposed that the reaction of methylamine with cosmic rays will form both of the isomers $NH_2CH_2^{\bullet}$ and $CH_3NH^{\bullet}$.[45] The question is whether the radical $NH_2CH_2^{\bullet}$ species is stable enough to effect the reaction shown in eqn (2) or whether it rearranges to $CH_3NH^{\bullet}$?

The interconversion between the isomers $NH_2CH_2^{\bullet}$ and $CH_3NH^{\bullet}$ has been studied at the CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory, and is shown in Fig. 1 with full energy and geometry data recorded in Table S1.† The two radicals have relative ΔG values of 0 and +18 kJ mol^{-1}, with an interconversion barrier of 177 kJ mol^{-1} (from $NH_2CH_2^{\bullet}$). This is a significant barrier and suggests that both radicals should be stable species. In order to determine experimentally whether $NH_2CH_2^{\bullet}$ is a stable species in the gas phase, we have carried out a neutralization/reionization study[46] of $^{+}NH_2{=}CH_2$ (formed by loss of $CH_3^{\bullet}$ from the ethylamine radical cation). This experiment involves the comparison of the collision induced (CID) mass spectrum (MS/MS) of $^{+}NH_2{=}CH_2$ with the neutralization/reionization spectrum ($^{+}NR^{+}$) of $^{+}NH_2{=}CH_2$ (the positive ion spectrum of the neutral $NH_2CH_2^{\bullet}$ formed by electron capture from $^{+}NH_2{=}CH_2$). If the two spectra are different, then some rearrangement or decomposition of neutral $NH_2CH_2^{\bullet}$ has occurred during the microsecond duration of the neutralization/reionization experiment. If the two spectra are the same the radical species is stable for the duration of the experiment. The two spectra are shown in Fig. 2. Apart from the different abundances of the $(M–H^{\bullet})^{+}$ ions (*m/z* 29), the spectra are very similar. Thus a combination of theory and experiment suggests the radical $NH_2CH_2^{\bullet}$ should be a stable species in interstellar media, and eqn (2) to be a plausible method for the synthesis of NH_2CH_2CN.

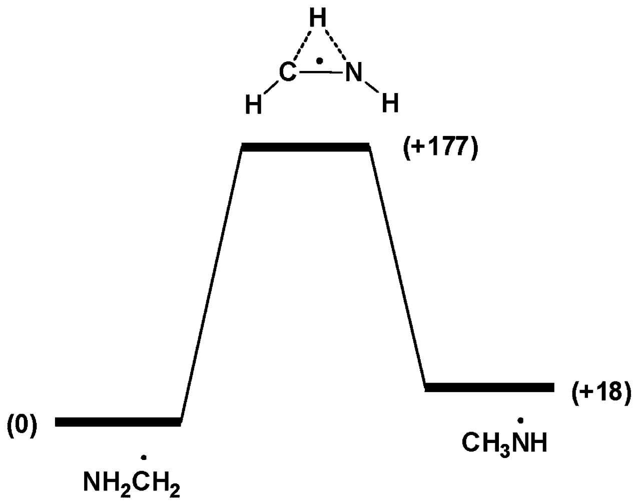

Fig. 1 The interconversion of $NH_2CH_2^{\bullet}$ and $CH_3NH^{\bullet}$. CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory. ΔG relative values are in kJ mol^{-1}. For full energy and geometry data of minima and transition state see Table S1.†

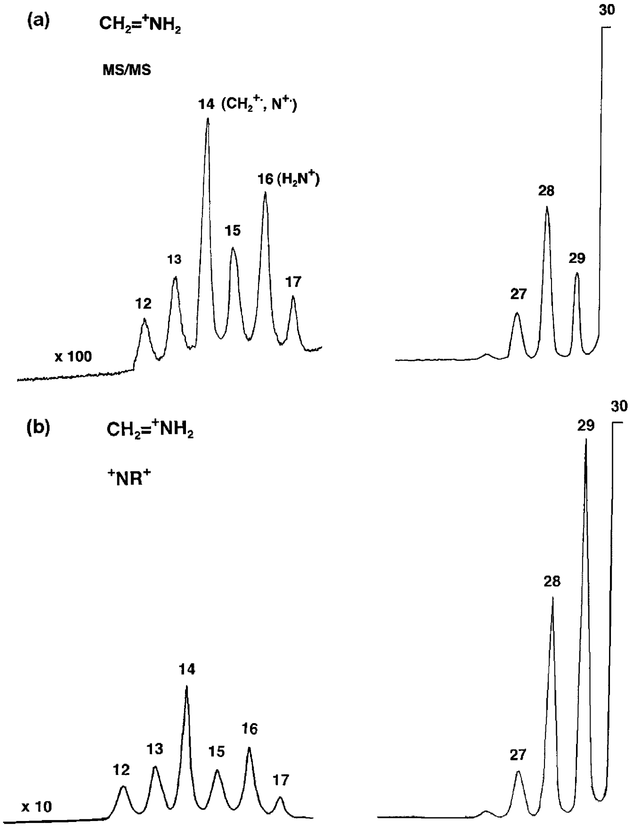

Fig. 2 (a) CID MS/MS data for $^{+}NH_2{=}CH_2$. (b) $^{+}NR^{+}$ spectrum of $^{+}NH_2{=}CH_2$. ZAB 2HF mass spectrometer. For experimental conditions see Experimental Section.

2. The formation of $NH_2^{\bullet}CHCN$

In order to form $NH_2CH(R)CN$ by radical combination we need a suitable synthesis of the precursor radical $NH_2^{\bullet}CHCN$. The reactions shown in eqns (3) to (5) would appear to be possible processes.

$$NH_2CH_2CN \rightarrow NH_2{}^{\bullet}CHCN + H^{\bullet}\ (+406\ \text{kJ mol}^{-1}) \quad (3)$$

$$NH_2CH_2CN + H^{\bullet} \rightarrow NH_2{}^{\bullet}CHCN + H_2\ (-101\ \text{kJ mol}^{-1}) \quad (4)$$

$$NH_2CH_2CN + HO^{\bullet} \rightarrow NH_2{}^{\bullet}CHCN + H_2O\ (-130\ \text{kJ mol}^{-1}) \quad (5)$$

Eqn (3) is unfavourable and would need to be initiated by irradiation, (*cf.*[45]) whereas the other two processes involve favourable radical abstractions. The reaction coordinate profile of the reaction summarized in eqn (5) is shown in Fig. 3 with full energy and geometry data for minima and transition state structures recorded in Table S2.† The reaction is feasible, with a barrier of 41 kJ mol^{-1} to the transition state; the overall process is favourable with $\Delta G = -130$ kJ mol^{-1}.

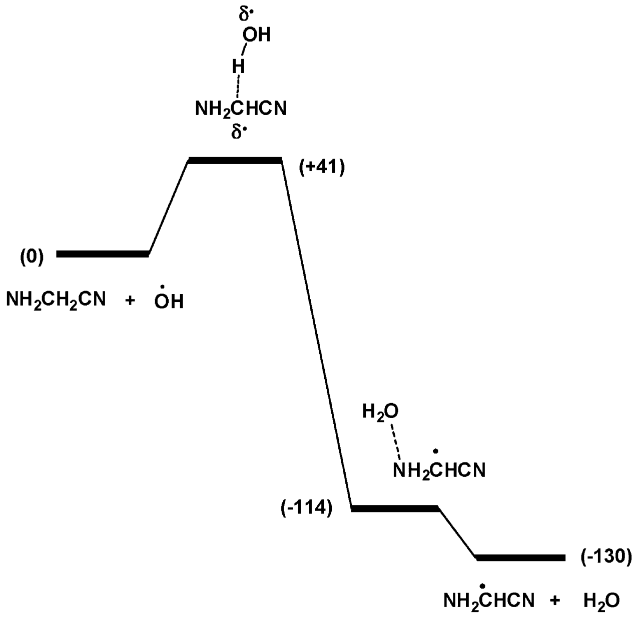

Fig. 3 Reaction coordinate profile of the reaction between NH_2CH_2CN and $HO^{\bullet}$. CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory. ΔG relative values are in kJ mol^{-1}. For full energy and geometry data of minima and transition state see Table S2.†

3. The formation of $NH_2CH(CH_2OH)CN$: a Ser precursor

The proposal for the formation of the Ser precursor is the radical/radical coupling reaction shown in eqn (6).

$$NH_2{}^{\bullet}CHCN + {}^{\bullet}CH_2OH \rightarrow NH_2CH(CH_2OH)CN\ (-240\ \text{kJ mol}^{-1}) \tag{6}$$

The hydroxymethyl radical has not been detected in interstellar regions, but methanol and $CH_2{=}^{+}OH$ have,[29] and it has been proposed that $^{\bullet}CH_2OH$ may be formed by the interaction of methanol with cosmic rays.[45] The stability of the hydroxymethyl radical has been demonstrated in a previous study.[47] Calculations at the CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory indicate that the isomers $^{\bullet}CH_2OH$ (0 kJ mol^{-1}) and $CH_3O^{\bullet}$ (+29 kJ mol^{-1}) are connected by a transition state with a significant barrier (+177 kJ mol^{-1}).[47] In addition, the CID MS/MS and $^{+}NR^{+}$ of $CH_2{=}^{+}OH$ (formed from the ethanol radical cation by loss of $CH_3{}^{\bullet}$) are characteristic of the structure, and very similar.[47] The reaction summarized in eqn (6) is barrierless, with $\Delta G = -240$ kJ mol^{-1}.

4. The formation of $NH_2CH(CH_2SH)CN$: a Cys precursor

The proposal for the formation of the Cys precursor is the radical/radical coupling reaction shown in eqn (7).

$$NH_2{}^{\bullet}CHCN + {}^{\bullet}CH_2SH \rightarrow NH_2CH(CH_2SH)CN\ (-227\ \text{kJ mol}^{-1}) \tag{7}$$

$$CH_3SH \rightarrow {}^{\bullet}CH_2SH + H^{\bullet}\ (+373\ \text{kJ mol}^{-1}) \tag{8}$$

The mercaptomethyl radical has not been identified in interstellar regions, but methyl mercaptan has,[29] and it is proposed that the $^{\bullet}CH_2SH$ may be formed from methyl mercaptan by ultraviolet or cosmic ray interaction as shown in eqn (8). The reaction coordinate for interconversion of the two isomers $^{\bullet}CH_2SH \rightarrow CH_3S^{\bullet}$ is shown in Fig. 4 (see also Table S3†), and shows a barrier (+114 kJ mol^{-1}) from $^{\bullet}CH_2SH$, a value less than that shown in Fig. 1. This raises the question as to whether these two species may equilibrate in interstellar dust clouds.

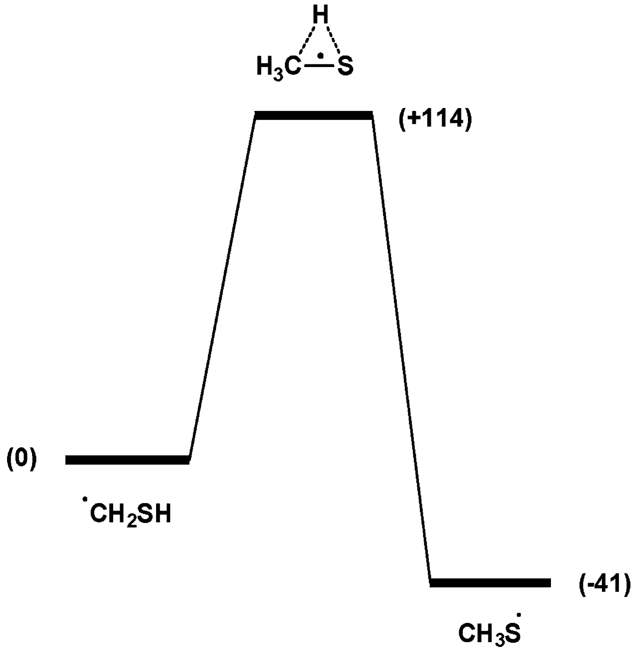

Fig. 4 The interconversion of $^{\bullet}CH_2SH$ and $CH_3S^{\bullet}$. CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory. ΔG relative values are in kJ mol^{-1}. For full energy and geometry data of minima and transition state see Table S4.†

Since the theoretical data are equivocal concerning interconversion of the two isomers; the question of stability needs to be settled by experiment. In this experiment the anions $^{-}CH_2SH$ (from $HSCH_2CO_2{}^{-}$) and CH_3S^{-} (from the reaction of HO^{-} with CH_3SSCH_3) are used to produce charge reversal ($^{-}CR^{+}$, synchronous two electron stripping of the anion to the decomposing cation),[48] and neutralization/reionization ($^{-}NR^{+}$, two step sequential charge stripping, first to the neutral and then loss of the second electron from the neutral to form a decomposing cation).[46] In these cases comparison of the $^{-}CR^{+}$ and $^{-}NR^{+}$ spectra will indicate the stability (or otherwise) of the neutrals; if the two spectra are identical, the neutral is stable for the microsecond timeframe of the neutralization/reionization process, whereas if the $^{-}NR^{+}$ spectrum is different from the analogous $^{-}CR^{+}$ spectrum, the neutral is rearranging and/or dissociating within the microsecond timeframe of the experiment. The $^{-}NR^{+}$ spectra are shown in Fig. 5 and 6. The $^{-}NR^{+}$ spectrum of $^{-}CH_2SH$ is different

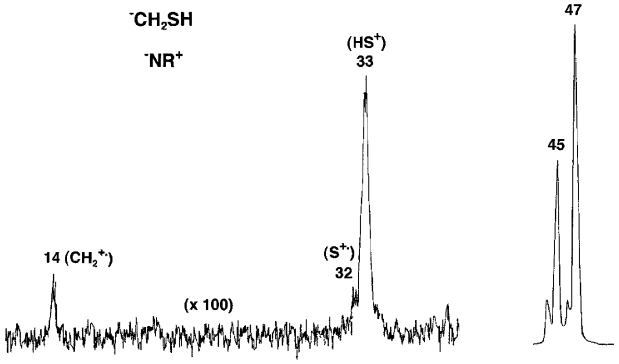

Fig. 5 $^-NR^+$ mass spectrum of $^-CH_2SH$. ZAB 2HF mass spectrometer. For experimental conditions see Experimental Section. $^-CR^+$ spectrum of $^-CH_2SH$[49] [*m/z* (product) abundance (%)]; 47(parent)100; 46(parent - $H^\bullet$)26; 45(parent - H_2)55; 33(HS^+)5; 32($S^{+\bullet}$)56; 15(CH_3^+)2; 14($CH_2^{+\bullet}$)22; 13(CH^+)2, 12($C^{+\bullet}$)1.

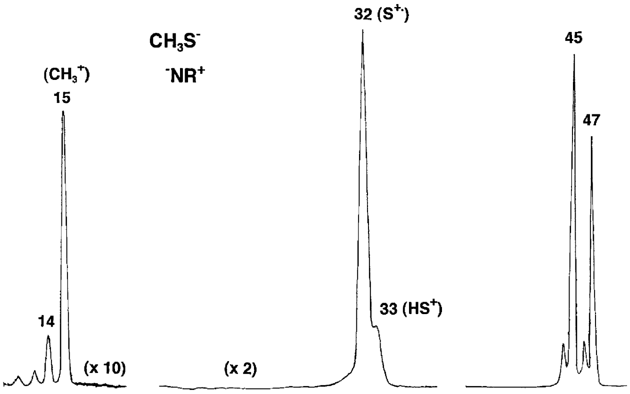

Fig. 6 $^-NR^+$ mass spectrum of CH_3S^-. ZAB 2HF mass spectrometer. For experimental conditions see Experimental Section. $^-CR^+$ spectrum of CH_3S^-[49] [*m/z* (product) abundance (%)]; 47(parent)66; 46(parent - $H^\bullet$)24; 45(parent - H_2)100; 33(HS^+)56; 32($S^{+\bullet}$)8; 15(CH_3^+)9; 14($CH_2^{+\bullet}$)3; 13(CH^+)2, 12($C^{+\bullet}$)1.

from that of CH_3S^-. In addition, the $^-CR^+$ (see captions to Fig. 5 and 6; also [49]) and $^-NR^+$ spectra in each system are virtually the same, indicating that $^\bullet CH_2SH$ and $CH_3S^\bullet$ do not rearrange under the experimental conditions. Thus the synthetic sequence shown in eqn (7) is feasible.

5. Formation of $NH_2CH(CH_2CN)CN$: An Asp precursor

Finally, the precursor to Asp [$NH_2CH(CH_2CO_2H)CO_2H$], can in principle, be formed from $NH_2CH(CH_2CN)CN$, which in turn can be made by the radical coupling reaction shown in eqn (9).

$$\begin{gathered} NH_2{}^\bullet CHCN + {}^\bullet CH_2CN \rightarrow \\ NH_2CH(CH_2CN)CN\ (-223\ \text{kJ mol}^{-1}) \end{gathered} \tag{9}$$

The reaction shown in eqn (9) requires the presence of a stable acetonitrile radical. This radical has been shown to be stable in a previous study using both theoretical and experimental studies.[44] However, both the acetonitrile and acetoisonitrile radicals are interstellar molecules and the question arises as to their integrity. The reaction coordinate of the $^\bullet CH_2CN$/$^\bullet CH_2NC$ interconversion is shown in Fig. 7, with full details of minima and transition states listed in Table S4.† Fig. 7 indicates that $^\bullet CH_2CN$ should essentially be stable, but that some $^\bullet CH_2NC$ molecules might convert to

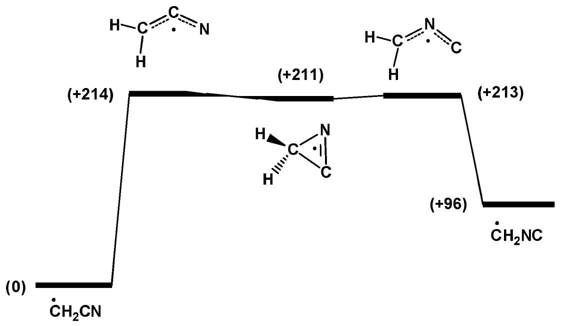

Fig. 7 The interconversion of $^\bullet CH_2CN$ and $^\bullet CH_2NC$. CCSD(T)/aug-cc-pVDZ//B3LYP/6-31+G(d) level of theory. ΔG relative values are in kJ mol^{-1}. For full energy and geometry data of minima and transition state see Table S5.†

$^\bullet CH_2CN$ (*i.e.* the forward and reverse barriers are + 214 and +117 kJ mol^{-1} respectively).

Conclusions

The application of theory and experiment in concert indicates that, at least for precursors of Ser, Cys and Asp, radical/radical coupling between $NH_2{}^\bullet CHCN$ and $R^\bullet$ ($R^\bullet$ = $^\bullet CH_2OH$, $^\bullet CH_2SH$ and $^\bullet CH_2CN$) is feasible in gas phase conditions. Such syntheses do not account for the predominant use of the L enantiomers of amino acids in biological systems.

Experimental section

A. Mass Spectrometric Methods

The experiments were performed using a two-sector modified VG ZAB 2HF mass spectrometer with **BE** configuration, where **B** and **E** represent magnetic and electric sectors, respectively. The precursor ions $CH_2{=}^+NH_2$, $^-CH_2SH$ and CH_3S^- were formed in the chemical ionization source from the ethylamine molecular cation, the thioglycolate anion ($HSCH_2CO_2^-$) and reaction of HO^- on CH_3SSCH_3. Source conditions were as follows:- source temperature 100 °C, repeller voltage –0.5 V, ion extraction voltage 7 kV, mass resolution $m/\Delta m \geq 1500$. For the formation of the precursor ions, the appropriate neutral was added through the septum inlet (unheated) to give a pressure of 10^{-5} Torr measured in the source housing. In the cases of the two anions, water (the precursor of HO^-) is then introduced through the septum inlet (unheated) to give a constant pressure of 10^{-4} Torr in the source housing: the estimated pressure in the ion source is 10^{-1} Torr. Collision induced (CID) spectra were determined using the magnetic sector to select the parent ion, utilising oxygen as the collision gas in the first collision cell following the magnetic sector. The pressure of oxygen in the first cell was maintained such that 80% of the parent ion beam was transmitted through the cell. This corresponds to an average of 1.1–1.2 collisions per ion.[50] Product cation peaks resulting from CID, $^-CR^+$ and $^-NR^+$ processes were recorded by scanning the electric sector.

Neutralization/reionization spectra ($^+NR^+$ or $^-NR^+$)[46] were performed for mass selected ions utilizing the dual collision cells located between the magnetic and electric sectors. Neutralization of cations or anions was effected by collisional electron attachment or detachment using O_2 at 80% transmission (of the ion beam) as collision gas in the first collision cell, while reionization to cations was achieved by collision of neutrals with O_2 (80% transmission) in the second collision cell. To detect a reionization signal due to the parent neutral, the neutral species must be stable for the one microsecond timeframe of this experiment. Charge reversal ($^-$CR$^+$) spectra[48] were recorded using single-collision conditions in collision cell 1 (O_2, 80% transmission of main beam). Comparison of $^-$CR$^+$ and $^-$NR$^+$ (or CID and $^+$NR$^+$) data for a given parent anion provides information concerning the neutral formed from the parent anion: see[46] for descriptions of this procedure.

B. Theoretical methods

Geometry optimizations were carried out at the B3LYP/6-31+G(d) level of theory,[51] within the GAUSSIAN 03 suite of programs.[52] Stationary points were characterized as either minima (no imaginary frequencies) or transition states (one imaginary frequency) by calculation of the frequencies using analytical gradient procedures. The minima connected by a given transition structure were confirmed by intrinsic reaction coordinate (IRC) calculations.[53] The calculated frequencies were also used to determine zero-point vibrational energies which were then scaled by 0.9804[51] and used as a zero point correction for electronic energies. More accurate energies for the B3LYP geometries were determined using the CCSD(T)/aug-cc-pVDZ level of theory[54] including zero-point energy correction (calculated by vibrational frequencies at the B3LYP/6-31+G(d) level of theory). ΔG values recorded in the text or a figure are calculated at 298 K. All calculations were carried out using eResearch [the South Australian Partnership for Advanced Computing (SAPAC) Facility], and the Australian Partnership for Advanced Computing (APAC) [Australian National University (Canberra)] facilities.

Acknowledgements

This project was funded by a grant from the Australian Research Council. TW thanks the ARC for a research associateship. We thank eResearch [the South Australian Partnership for Advanced Computing (SAPAC) Facility], and the Australian Partnership for Advanced Computing (APAC) [Australian National University (Canberra)] for generous allocations of supercomputing time.

References

1 L. E. Snyder, *Origins Life Evol. Biosphere*, 1997, **27**, 115.
2 A. Brack (ed.), *The molecular origin of life*. Cambridge University Press, New York, 1998.
3 H. S. Zhu and J. J. Ho, *J. Phys. Chem. A*, 2004, **108**, 3798.
4 J. R. Cronin and S. Pizzarello, *Adv. Space Res.*, 1983, **3**, 5.
5 J. R. Cronin and S. Chang, in J. M. Greenberg, V. Pirronello and C. Mendoza-Gomez, eds, *Chemistry of Life's Origins* (NATO ASI), 1993, pp. 209–258, Kluwer, Dordrecht.
6 S. P. Walch and E. L. O. Bakes, *Chem. Phys. Lett.*, 2001, **346**, 267.
7 D. E. Woon, *Astrophys. J.*, 2002, **571**, L177.
8 G. Botta, D. P. Glavin, G. Kminek and J. L. Bala, *Origins Life Evol. Biosphere*, 2002, **32**, 143.
9 S. L. Miller, *Science*, 1953, **117**, 528; A. P. Johnson, H. J. Cleaves, J. P. Dworkin, D. P. Glavin, A. Lazcano and J. L. Bada, *Science*, 2008, **322**, 404.
10 Y. Takano, A. Ohashi, T. Kaneko and K. Kobayashi, *Appl. Phys. Lett.*, 2004, **84**, 1410.
11 M. P. Bernstein, J. P. Dworkin, S. A. Sandford, G. W. Cooper and L. J. Allamandola, *Nature*, 2002, **416**, 401.
12 G. M. Munoz Caro, U. L. Melerhenrich, W. A. Schutte, B. Barbler, A. A. Segovia, H. Rosenbaure, W. H.-P. Thiemann, A. Brack and J. M. Greenberg, *Nature*, 2002, **416**, 403.
13 R. D. Brown, P. D. Godfrey and J. W. V. Storey, *Mon. Not. Roy. Astrom. Soc.*, 1979, **186**, 5P.
14 J. M. Hollis, L. E. Snyder, R. D. Suenram and F. J. Lovas, *Astrophys. J.*, 1980, **241**, 1001.
15 L. E. Snyder, J. M. Hollis, F. J. Suenram, F. J. Lovas, L. W. Brown and D. Buhl, *Astrophys. J.*, 1983, **268**, 123.
16 I. I. Berulis, S. A. Sandford and L. J. Allamandole, *Sov. Astro. Lett.*, 1985, 251.
17 M. Guelin and J. Cernicharo, in G. Winnewisser and T. Arstrong ed., *Physics and Chemistry of Interstellar Molecular Clouds*, Springer-Verlag, Berlin, 1989, 337.
18 F. Combes, N.-Q. Rieu and G. Wlodarszak, *Astron. Astrophys.*, 1996, **308**, 618.
19 C. Ceccarelli, L. Loinard, A. Castets, A. Faure and B. Lefloch, *Astron. Astrophys.*, 2000, **362**, 1122.
20 J. M. Hollis, J. A. Pedalty, L. E. Snyder, P. R. Jewell, F. J. Lovas, P. Palmer and S. Y. Lie, *Astrophys. J.*, 2003, **588**, 353.
21 J. Crovisier, D. Bockelee-Morvan, P. Colom, N. Biver, D. Despois and D. C. Lis, *Astron. Astrophys.*, 2004, **418**, 1141.
22 P. Ehrefreund, M. P. Berstein, J. P. Dworkin, S. A. Sandford and L. J. Allamandola, *Astrophys. J.*, 2001, **550**, L95.
23 M. P. Bernstein, S. F. M. Ashbourne, S. A. Sandford and L. J. Allamandola, *Astrophys. J.*, 2004, **601**, 365.
24 S. B. Charley, P. Ehrenfreund and Y-. J. Kuan, *Spectrochim. Acta, Part A*, 2001, **57**, 685.
25 Y.-J. Kuan, S. B. Charnley, H. C. Huang, W. L. Tseng and Z. Kisiel, *Astrophys. J.*, 2003, **593**, 848.
26 L. E. Synder, F. J. Lovas, J. M. Hollis, D. N. Friedel, P. R. Jewell, A. Remijan, V. V. Ilyushin, E. A. Alexseev and S. F. Dyubko, *Astrophys. J.*, 2005, **619**, 914.
27 D. Smith and P. Spanel, *Mass Spectrom. Revs.*, 1995, **14**, 225; G. Winnewisser and C. Kramer, *Space Sci. Rev.*, 1999, **90**, 181; S. B. Charley, P. Ehrenfreund and Y.-J. Kuan, *Spectrochim. Acta, Part A*, 2001, **57**, 685.
28 A. Belloche, K. M. Menten, C. Comito, H. S. P. Mueller, P. Schilke, J. Ott, S. Thorwirth and C. Hieret, *Aston. Astrophys.*, 2008, **492**, 769.
29 A. Wootten, http://www.cv.nrao.edu/~awootten/allmols.html.
30 O. Botta, D. P. Glavin, G. Kminek and J. L. Bada, *Origins Life Evol. Biosphere*, 2002, **32**, 143.
31 R. Arnaud, C. Adamo, M. Cossi, A. Milet, Y. Valleé and V. Barone, *J. Am. Chem. Soc.*, 2000, **122**, 324.
32 V. A. Basiuk, *J. Phys. Chem. A*, 2001, **105**, 4252.
33 A. Strecker, *Liebigs Ann. Chem.*, 1850, **75**, 27.
34 D. E. Woon, *Int. J. Quantum Chem.*, 2002, **88**, 226.
35 A. Largo, P. Redondo and C. Barrientos, *Int. J. Quantum Chem.*, 2004, **98**, 355.
36 H. M. Boechat-Roberty, S. Pilling and A. C. F. Santos, *Astron. Astrophys.*, 2005, **438**, 915.
37 M. T. Feldmann, S. L. Widicus, G. A. Blake, D. R. Kent and W. A. Goddard, *J. Chem. Phys.*, 2005, **123**, 34304.
38 V. Biagojevic, S. Petrie and D. K. Bohme, *Mon. Not. R. Astron. Soc.*, 2003, **339**, L7.
39 D. M. Jackson, N. J. Stibrich, N. G. Adams and L. M. Badcock, *Int. J. Mass Spectrom.*, 2005, **243**, 115.
40 S. P. Walch and E. L. O. Bates, *Chem. Phys. Lett.*, 2001, **346**, 267.
41 P. D. Holton, C. J. Bennett, Y. Osanuna, N. J. Mason and R. I. Kaiser, *Astrophys. J.*, 2005, **626**, 940.
42 W. H. Sorrell, *Astrophys. J.*, 2001, **555**, L129.
43 V. A. Basiuk and Y. Kobayashi, *Int. J. Quantum Chem.*, 2004, **99**, 91.
44 H. J. Andreazza, M. Fitzgerald and J. H. Bowie, *Org. Biomol. Chem.*, 2006, **4**, 2466.
45 P. D. Holtom, C. J. Bennett, Y. Osamura, N. J. Mason and R. I. Kaiser, *Astrophys. J.*, 2005, **626**, 940.
46 C. Wesdemiotis and F. W. McLafferty, *Chem. Rev.*, 1987, **87**, 485; D. V. Zagorevskii and J. L. Holmes, *Mass Spectrom. Rev.*, 1994, **13**, 133; N. Goldberg and H. Schwarz, *Acc. Chem. Res.*, 1994, **13**, 133; C. A. Shalley, G. Hornung, D. Schröder and H. Schwarz, *Int. J. Mass Spectrom. Ion Processes*, 1998, **172**, 181; D. V. Zagorevskii and J. L. Holmes, *Mass Spectrom. Rev.*, 1999, **18**, 87.

47 T. Wang and J. H. Bowie, *Org. Biomol. Chem.*, 2010 submitted for publication DOI: 10.1039/c00125b.

48 J. H. Bowie and T. Blumenthal, *J. Am. Chem. Soc.*, 1975, **97**, 2959; J. E. Szulejko, J. H. Bowie, I. Howe and J. H. Beynon, *Int. J. Mass Spectrom. Ion Phys.*, 1980, **34**, 99; M. M. Bursey, *Mass Spectrom. Rev.*, 1990, **9**, 555.

49 K. M. Downard, J. C. Sheldon, J. H. Bowie, D. E. Lewis and R. N. Hayes, *J. Am. Chem. Soc.*, 1989, **111**, 8112.

50 J. L. Holmes, *Org. Mass Spectrom.*, 1985, **20**, 169.

51 A. D. Becke, *J. Chem. Phys.*, 1993, **98**, 5648; P. J. Stephens, F. J. Devlin, C. F. Chablowski and M. J. Frisch, *J. Phys. Chem.*, 1994, **98**, 11623.

52 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Topyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Makajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Know, H. P. Hratchian, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austlin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Cliffors, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Latham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03*, Revision E; Gaussian, Inc.: Wallingford, CT, 2004.

53 K. Fukui, *Acc. Chem. Res.*, 1981, **14**, 363; C. Gonzalez and H. B. Schlegel, *J. Chem. Phys.*, 1989, **90**, 2154; C. Gonzalez and H. B. Schlegel, *J. Phys. Chem.*, 1990, **94**, 5523.

54 T. H. Dunning, *J. Chem. Phys.*, 1989, **90**, 1007; D. E. Woon and T. H. Dunning, *J. Chem. Phys.*, 1993, **98**, 1358.