Hunt for Molecules
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BIOLOGICAL MOLECULES

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Abstract. Many molecules involved in current models of prebiotic chemistry have been found in meteorites and, to a lesser extent, in the interstellar medium and comets. We review here some recent results and some early developments from radio astronomy. New instruments like ALMA, and new techniques, like sample analysis in the lab of cometary or interstellar grains will improve our knowledge of the nature of extraterrestrial molecules which may have contributed to the initial stock of prebiotic molecules on the early Earth. A precise quantitative estimate of this contribution should be the ultimate goal.

In 1976, when I started working in the radio astronomy department of Meudon Observatory, P.Encrenaz kindly gave me a copy of his recently published little book on Interstellar molecules. I was then concerned by OH, a very small molecule. But the reading of the chapter of this book on biological molecules contributed to arise my own present interest for their quest in ISM and comets.

1 Introduction

Biological molecules, which may be defined as molecules present in cells, are of importance to astronomers in two contexts: the search for life elsewhere (biomarkers), and the origin of life on Earth (prebiotic molecules). I will discuss here only the latter aspect.

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A common hypothesis on the origin of life on Earth is nowadays that life started from a pool of more or less complex species, and, when the initial stock was out, developed biosynthetic pathways to produce them. The nature and origin of this first pool of molecules is one of the central questions of Exobiology, or Astrobiology, an interdisciplinary effort to understand the origin, evolution and distribution of life on Earth and in the Universe. Three main sources of molecules are presently studied: atmospheric, hydrothermal, and "extraterrestrial". What is meant by "extraterrestrial source" is a process delivering molecules to the early Earth via solar sytem bodies. These bodies can span a broad range of sizes —from dust particles to comets and asteroids— and contain carbon compounds originally synthesized either in the body itself, in the Solar nebula or inherited from the interstellar medium. The three sources are not exclusive, each may have contributed to a certain extent still to be determined. Before addressing the extraterrestrial source, let us say a few words on the two other sources.

The possibility of chemical synthesis of prebiotic compounds in a planetary atmosphere was demonstrated by the well known Urey-Miller experiment (Miller 1953). This experience has founded many developments in exobiology, but has been considered for a long time irrelevant to the case of the Earth itself. Planetologists (eg Kasting 1993) have namely favoured a neutral composition (eg CO_2, N_2, H_2O) for the atmosphere of the early Earth rather than the reducing gases CH_4,NH_3, H_2O used by Miller. This is not favourable for atmospheric synthesis (see eg Raulin 2005, Table 2.2). However very recently Tian et al (2005) proposed a reevaluation of the H_2 content of the early Earth atmosphere. The new higher value reintroduces the atmophere as a potential important place for the synthesis of prebiotic organic compounds.

Hydrothermal systems have also been early proposed as sites for abiotic synthesis of carbon compounds (French, 1962). Hydrothermal circulation occurs for example when seawater percolates through fractured ocean crust along the mid-ocean ridge (eg German 2004). This seawater is first heated (up to 400 ^{o}C), dissolves minerals, and eventually merges again into cold (2^{o}C) seawater . Difficult experiments are conducted to establish the effective yield in carbon compounds of such natural chemical reactors(Holm and Anderson, 2005); but high temperatures may also destroy organic compounds (Lazcano and Miller, 1996). Elaborate but still very hypothetical scenarios of origin of life from ocean hydrothermal system have been proposed (Russel, 2006).

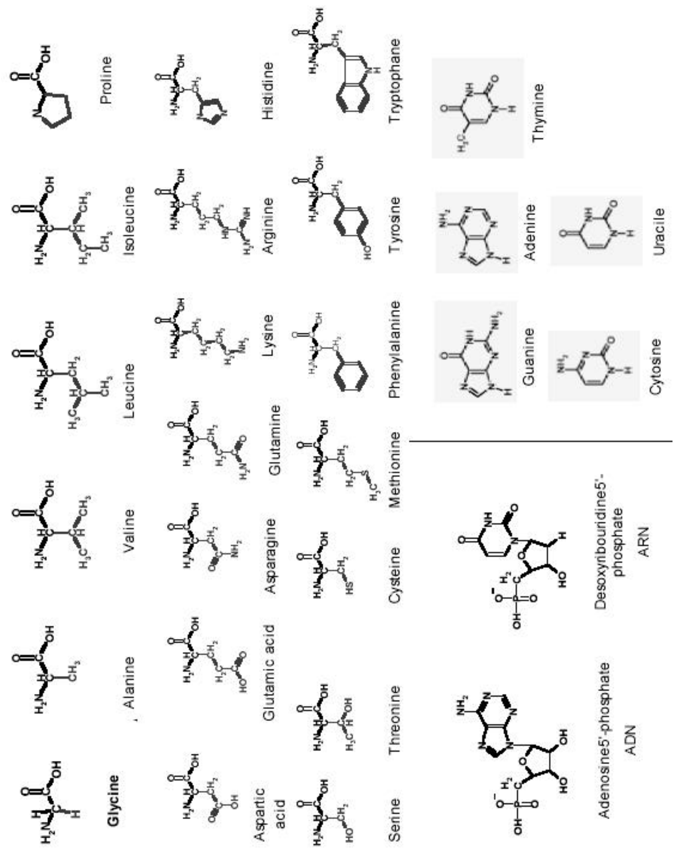

Fig. 1. Some biological molecules which may be sought for in the ISM and in solar system small bodies: a) glycine and the 19 other proteic amino acids b) examples of nucleotides (base+(desoxy)ribose+phosphate) and the 5 nucleic RNA and DNA bases

2 Which molecules can we call "prebiotic" ? where do they come from ?

No molecule (except perhaps water) can be considered at present a compulsory element of prebiotic chemistry, as this is model-dependent and no scenario is universally accepted. However a few species are often quoted, due to their chemical properties, their likely large abundance on the early Earth, or their key role in modern cells.

A first group includes "small reactive molecules" like HCN, H_2CO, HC_3N, NH_3, ... These small molecules form the basis of a (often aqueous) prebiotic chemistry which can lead to more complex molecules through a set of reactions like the Strecker synthesis of amino-acids (NH_3, RCHO and HCN react to form NH_2-CRH-COOH), Bucherer-Berg synthesis, formose reaction (sugars are formed from H_2CO) , or reactions leading to nucleic bases, eg adenine ($H_5C_5N_5$) synthesis from HCN as proposed by Oró (for more on these topics cf Brack and Raulin 1991, Raulin et al. 2005, Commeyras et al. 2005).

A second group includes the building blocks (monomers) of the important biopolymers. Amino acids (Fig 1a) are the building blocks of proteins , nucleotides (Fig 1b) those of nucleic acids DNA and RNA, while fatty acids (eg Fig 2b) assemble to form the lipidic membrane.

It is however often considered that several of these molecules require already complex steps to be formed, which leads to focus on smaller units: nucleotides are formally the assembly of a phosphate group, a C5 cyclic sugar (ribose or desoxyribose) and a nuclear base. The latter molecules, their related species and precursors are indeed the prebiotic compounds whose possible existence on the early Earth is investigated.

It should be however kept in mind that this "Lego" approach is not the only possible one: present day synthesis of nucleotides does not proceed by "sticking together" a phosphate, a ribose and a nucleic base, which at least raises the question of the validity of such a scheme under prebiotic conditions. More generally, an important concept is "uptake": if a given function in the cell is nowadays performed by a given molecule, the simplest is of course that this molecule played this role from the start; but conceivably older pathways or compounds may have been replaced by newer ones.

Beside DNA and AA other molecules are present in all or allmost all known living cells. Coenzymes, which accompany proteins in their catalytic function are an such example.The complex structure of Coenzyme A (Fig 2) is at present not explained by selection effects (Keefe et al. 1995) ; this may suggest it appeared as an opportunistic construction from abundant prebiotic subunits. This would suggest for example the search for alphaketoisovaleric acid (Fig 2) in meteorites and ISM. This is however highly speculative and is probably close to the upper limit in complexity for extraterrestrial

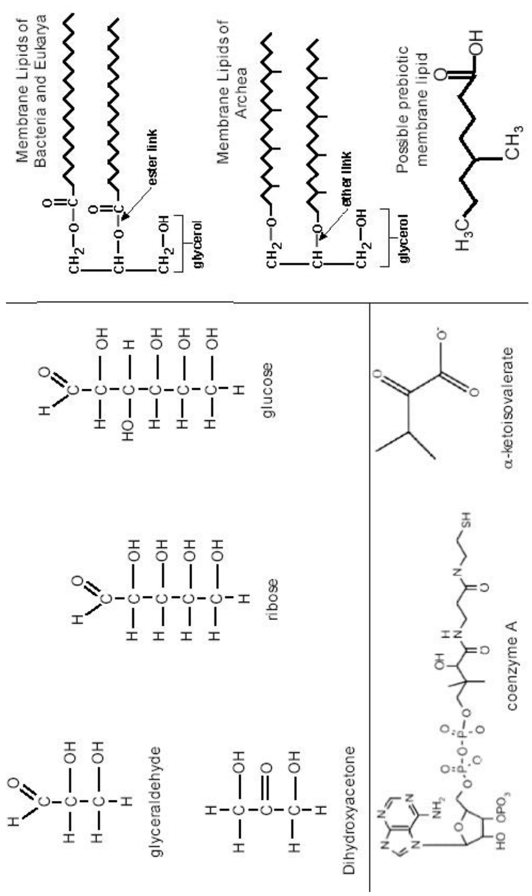

Fig. 2. Other biological molecules which may be sought for in the ISM and in solar system small bodies: a) sugars in C3(DHA, glyceraldehyde), C5 (ribose), C6(glucose) b) some membrane lipids c) coenzyme A with one possible prebiotic precursor

molecules which might have directly influenced the choice of a molecule by early life chemistry.

Object	Reference	Result
SgrB2,OriA + 7 IS clouds	Brown et al. 1979	limit
Ori A, W51, SgrB2, IRC10216	Hollis et al. 1980	limit gly I (1 line ?)
18 gal. Sources + 1 comet	Snyder et al. 1983	limit gly II
Ori A, W51, SgrB2	Beralis et al. 1985	limit gly II
OriA, SgrB2, W3(OH)	Guelin Cernicharo 1989	limit gly I
OriA + SgrB2(OH)	Combes et al.1996	limit gly I and II
various IS sources	Snyder 1997 (review)	limits
IRAS16293	Ceccarelli et al. 2000	limit gly I and II
OMC1	Hollis et al. 2003K	limit gly I
SgrB2,OriA,W51	Kuan et al. (2003)	gly I found ?
SgrB2,OriA,W51	Snyder (2005)	limit gly, methodology
comet Hale-Bopp	Crovisier et al 2004	limit gly I
meteorites (carb. chondrites)	Botta & Bada 2002 (review)	~ 10(-7) mol/g

Glycine I	NH2-CH2-COOH	searched
Glycine II	NH2-CH2-COOH	searched
Methyl carbamate	NH2-COOCH3	searched
aminoethanol	NH2-CH2-OH	searched
amninonitrile	NH2-CH2-CN	searched
formamide	NH2-CHO	found
methylamine	NH2-CH3	found
acetic acid	CH3-COOH	found

Fig. 3. a) Brief history of the radio astronomical search for glycine b) molecules related to glycine

3 A few historical landmarks

In the years 1968-1972 most small molecules important for aqueous prebiotic chemistry were found in the ISM: NH_3 and H_2O by Townes' group (Cheung et al. 1969a,b), H_2CO (Snyder et al. 1969), HCN (Buhl and Snyder 1970), HC_3N (Turner 1971) and discussions readily began on the possible implication for the Origin of life. In 1973 , in the book "Molecules in the Galactic environment" edited by Gordon and Snyder, four authors (Ponnamperuna, Anders, Morrison, Sagan) discuss already "biological implications". In 1974 P. Encrenaz devoted a chapter of his book "Les molecules interstellaires" to biological molecules. In 1980 a paper by Irvine et al. discusses already the link between IS molecules, comets and life, whereas another one in 1981 reports a first search for imidazole, an heterocycle present in several important biological molecules. At the Montremblant IAU Symposium, Turner (1980) proposes tentative identifications of U-lines by complex species like pyrrole. P.Encrenaz participated to two important searches for significant biological species : acetone, which is dicovered in 1987 (Combes et al.), and acetic acid for which upper limits were obtained in IS clouds (Wootten et al 1992; this molecule was finally detected by Mehringer et al in 1997). During this period Hoyle and coworkers (eg Hoyle & Wickramasinghe 1986) proposed their bacterial model of IS grains, based on gross similarities of bacteria and IS grain IR spectra. Difficult to prove or disprove completely by remote observing, this model is however considered as extremely unlikely.

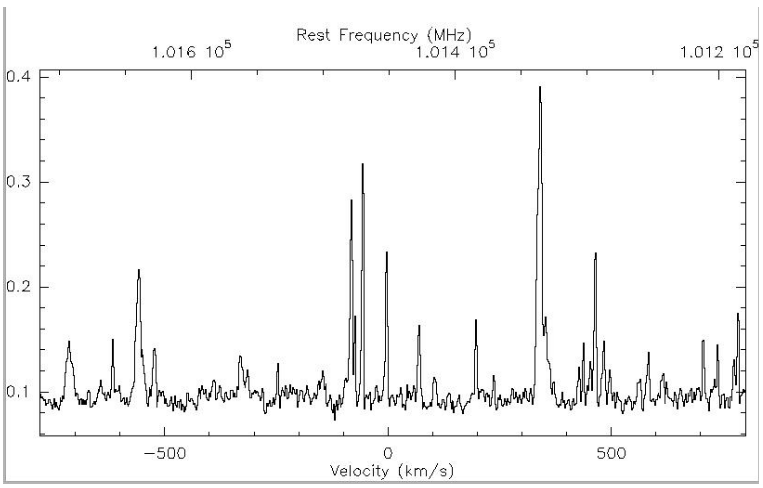

Fig. 4. Interferometric spectrum of Orion-KL taken at IRAM Plateau de Bure. All peaks are real lines (not noise !).

4 Recent results on complex and "biological" molecules in the ISM

Several groups are currently searching at radio wavelength for complex molecules of possible prebiotic interest. The first sugar (Dihydroxyacetone $(CH_2OH)_2CHO$) may have been detected toward SgR B2(N-LHM) by Widicus Weaver and Blake 2005; this follows the detection of the pre-sugar molecule glycolaldehyde (CH_2OHCHO) and of the related species CH_2OHCH_2OH (ethylene glycol) by Hollis et al. (2002) - the latter also detected in comets (Crovisier et al. 2004). Several N-bearing heterocycles have been searched for already (Charnley et al. 2005), and are proxies for nuclear bases. Glycine itself, NH_2CH_2COOH, whose discovery has been announced from searches (eg Kuan et al 2003), has been strongly questionned recently (Snyder et al. 2005). Table 1 lists a) some important steps in the glycine saga; b) a few species related to glycine, some of which have been found and other are being searched. The simpler acetic acid CH_3COOH has been found in several sources from BIMA observations of Hot cores by Remijan et al. (2004). Urea $(NH_3)_2CO$ has been tentatively detected from IS ices IR absorption spectra (Raunier et al. 2004). Recent GBT observations by Hollis et al (2004) have made complete the series propynal-propenal-propanal.

Some of these species are small cell metabolites, while the others can play a role in biomonomer synthesis under prebiotic conditions. In all cases the detection is difficult, and requires long integration times. In several cases an interferometer (BIMA) has been used to lower the confusion— but confusion still makes questionable some of these detections. How severe is the confusion problem is illustrated by Fig 4: only 3 channels of this 800 channels PDBI spectrum of Ori A have been considered devoid of any molecular emission (to the noise limit) based on a careful analysis of the interferometric maps !

5 Prospective

With large instruments soon to appear, and new techniques being developed, how many new molecules could we detect ? Which one to look for? Which techniques ?

5.1 Future investigation methods

Millimeter radiotelescopes (KPNO 12m, OSO 20m, IRAM 30m, CSO, JCMT) have been very succesful in detecting interstellar molecules . Biological molecules have large molecular weight ($>$ 100 amu) and large moments of inertia. They rotate slowly and could be best studied at lower frequencies ($<$ 100 GHz); beams are however larger at these frequencies, which may provoke excessive beam dilution. Several new ground based single dish telescopes are or will be soon in operation: Green Bank 110m Telescope (GBT) (already open up to to 45 GHz), the 45m LMT under construction in Mexico, and, for higher frequencies, the 12m APEX antenna close to ALMA site in Chile.

Sensitivity is not enough: spectral confusion is often the real limitation to the identification of new species. Molecules tend however to be grouped in spots corresponding to chemical families; these spots have a lower chemical diversity than the whole region. High spatial resolution brought by present and future radio interferometers allows to observe separately the spectra at each spot, which, taken individually, present less confusion. A further advantage is the possibility to adress molecule formation by studying their spatial distribution at places of varying physical conditions and ages. ALMA will be a key instrument, improving on the present interferometric studies with BIMA and PdBI but also OVRO and SMA and the future CARMA (joint BIMA-OVRO instrument). In a more remote timescale, the square kilometer array (SKA) interferometer can be a valuable tool if it can reach frequencies up to 20-30 GHz.

Some molecules can't be detected by pure rotational lines, because they lack a permanent dipole moment. For those, rovibrational transitions in the range of the submm space telescope Herschel/HIFI might be searched for.

Collection of samples of interstellar and solar system dust particles has already begun with the pioneering Stardust mission. Together with in situ analysis of comets (as planed with Rosetta lander) and asteroids (as in the Leonard project to an NEO under study) this will bring new insights in the molecules which can have been brought to Earth. A whole range of techniques like various kinds of chromatography and/or mass spectroscopy will be available. They will provide the only possible (though difficult) approach to the study of enantiomeric excess of chiral molecules - for which teledetection is not feasible in practice.

5.2 *which molecules?*

Molecules should be searched according to their potential significance in prebiotic chemistry on one hand, to their likely formation in extraterrestrial environments (ISM and protoplanetary discs) and transfer to the early Earth on the other hand.

Considering our present ideas on prebiotic chemistry, amino acids , simple sugars and nuclear bases are obvious targets. A high priority is to continue the search for glycine and related species, as they seem to be the easiest to detect (which does not mean easy !). Possibles precursors of glycine, like aminonitriles, could even be better candidates. Aminoacids with longer chains could then be searched, but the difficulty increases because of the expected lower abundances (many possible isomers, cf Kerridge 1999) , the complexity of the spectra (more numerous and fainter lines). Looking for larger sugars - after confirmation of DHA- is another obvious path. Some other molecules or molecule fragments appear to have an important biological role nowadays, which might be due to a relatively high abundance at early times: imidazole group, 5 and 6 atom heterocycles (see Charnley et al 2005), and possibly the coenzyme A precursors previously discussed.

How likely is the presence of these species in the ISM ? Chemical models are a first tool to consider . However the difficulty of such models increases rapidly with the number of species and the low abundance levels considered. Useful indications can also be obtained from asteroids(meteorites), comets and lab experiments. The analysis of meteorites is somewhat more advanced than that of ISM (500 vs 150 molecules), especially for compounds like aminoacids, of which 80 species have been already identified. Botta and Bada (2002) summarize the content determined for meteorites including the carbonaceous chondrite Murchison. However, the meteorite composition is not expected to be identical to ISM: in the protosolar nebula, as well as in the asteroid itself, further processing and formation of new species occured to an unknown extent .

Cometary composition is believed to be closer to ISM (Bockelée-Morvan et al 2000). But differences are also present (silicates, deuteration, ethylene glycol - eg Despois et al 2006). Up to now only ~ 30 molecules are identified from the ices (in fact from the sublimated ices in the coma) - and the composition of organic refractories remains unknown. A cumulative plot (Crovisier 2004) gives an indication on how many new species might be found in comets with improved sensitivity.

Lab experiments have been performed for a long time to simulate the evolution of interstellar ices under the effect of energy deposit from a heat source, from UV or X photons, or from energetic particles (protons or heavier nuclei) (see Cottin et al. 1999 for a review); recently some experiments have even been performed under circularly polarized light (Meierhenrich et al. 2001, Nuevo et al. 2004). Complex molecules are produced under such conditions, which may be sought for in solar system objects and/or IS clouds. For example Munoz-Caro et al. (2002) and Bernstein et al. (2002) recently reported the production of a variety of aminoacids. However, these experiments are not yet fully quantitative, and some compounds predicted to be abundant like HMT have yet resisted detection in natural objects. A further question is the possible presence in the experimental residue (and similarly in IS/SS matter) of only precursors of amino-acids - the latter being formed only in the analysis process.

6 Conclusion

The question of the contribution of extraterrestrial sources to Earth prebiotic chemistry is a difficult but well defined question. Identifying the molecules in the small bodies of the solar system and in the ISM is only a first step, for which interferometers like ALMA, in situ measurements in comets and asteroids, and sample return mission of small bodies (cometary matter including ices !) but also interstellar grains collected in the solar system (building up on Stardust pioneer attempt) will be decisive . Sample analysis will be required especially for chirality studies, which teledetection can hardly adress.

The next step will be to evaluate *quantitatively* how much material has effectively landed on Earth, which transformations, losses —and possibly gains— are due to the delivery process itself (atmospheric entry), how much of this solar system material is nebular and how much has been inherited from ISM , and what has been the real effective use by prebiotic chemistry of all the molecules delivered. This will refine the pioneer work made by Chyba and Sagan(1997) , and hopefully error bars will be obtained on these numbers. Only then will a balance of these results with comparable studies of atmospheric and hydrothermal chemistry on the early Earth be possible.

If the numerous complex species found in IS space appear to have played a major role in the origin of life on Earth, we will have already a basis to discuss the development of life on other planets. If not, if planetary sources dominate this step, the discussion will require to wait for statistical data on extrasolar terrestrial planets and for further numerous lab experiments and simulations.

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