

Is xenon an “ennobled” alkane?†

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Recent studies on liquid mixtures involving xenon and the light *n*-alkanes have revealed that, in many ways, xenon behaves like a member of the *n*-alkane family. The observed behaviour can be interpreted at the molecular level in terms of size and intermolecular potential. In this work the extension of this analogy to other microscopic and macroscopic properties is discussed. Furthermore, this behaviour is confirmed by the anaesthetic power of xenon relatively to those of the *n*-alkanes. We believe that this result might contribute to a better understanding of the mechanism of anaesthesia at the molecular level.

Introduction

Over one hundred years after xenon's discovery and its isolation from air by Sir William Ramsay,¹ and forty years after the preparation of its first compound,² XeF₂, this “strange” gas yields yet another surprise. Recent low temperature thermodynamic studies on liquid mixtures of xenon and the light *n*-alkanes seem to indicate that, at least in terms of phase equilibria, xenon behaves like a member of the *n*-alkane series.

This affinity was shown by the fact that liquid mixtures of xenon with ethane, propane and butane^{3,4} exhibit negative values both for the excess molar Gibbs energy, G^E , and excess molar volume, V^E . Higher *n*-alkanes also mix with negative G^E and V^E . The results suggested that the (xenon + *n*-alkanes) mixtures could be regarded as a special case of binary mixtures of *n*-alkanes and led us to a systematic investigation of mixtures of xenon with a variety of molecules (light *n*-alkanes and cycloalkanes,^{5,6} *n*-alkenes, perfluoroalkanes,^{7–9} boron halides,¹⁰ etc.). It was found that the behaviour of mixtures of an *n*-alkane with a second component is mirrored by that of xenon with that same component. For instance, mixtures of perfluorocarbons with normal hydrocarbons display the same liquid–liquid immiscibility that would occur in mixtures of xenon with perfluorocarbons, if solidification did not prevail.⁷

Further examples of the similarity between xenon and the *n*-alkanes in terms of phase equilibria, can be found in mixtures with alcohols,¹¹ namely methanol. Mixtures of ethane, propane and *n*-butane with methanol show type V phase behaviour in the scheme of Scott and van Konynenburg,¹² while methane displays type III phase behaviour. Similarly, it has been found that the (xenon + methanol) system also exhibits type V phase behaviour.

The predictive value of this evidence should not be underestimated. The properties of mixtures of *n*-alkanes with, say, a boron halide could then be deduced from the properties of the mixtures of xenon with that same halide. Moreover, due to its chemical inertia, high polarizability and convenient

liquid range, xenon has become more and more attractive as an ideal inert solvent.¹³ With a critical temperature around room temperature ($T_c = 289.7$ K) and a moderately high critical pressure ($p_c = 58.8$ bar), xenon can be easily liquefied. Additionally, solid xenon (below its triple-point, $T_t = 161.39$ K) provides a good matrix for the spectroscopic study of thermo-degradable molecules.

The extension of this analogy to other microscopic and macroscopic properties is discussed in this work. A final confirmation could be found in the field of anaesthesia, comparing the anaesthetic power of xenon relative to that of the *n*-alkanes.

Molecular properties and potentials

At this stage, a distinction should be made between low-density (dilute gas) and high-density (dense gas or liquid) fluids. The properties of the former are determined by the pair potential, $u(r)$, alone; those of the latter are very sensitive to fluid structure, which, in turn, is mainly determined by the repulsive forces (the so-called van der Waals idea). In dense fluids there is the added complication of multi-body interactions. These are usually dealt with through effective potentials, of which the Lennard–Jones intermolecular function is the prime example for simple (quasi-spherical) molecules.

A theoretical interpretation of our experimental results for mixtures of xenon with a variety of hydrocarbons was attempted using the statistical associating fluid theory for potentials of variable attractive range (SAFT-VR).^{14,15} In this approach molecules are modelled as strings of m hard spherical cores of diameter σ , with the attractive interactions described (in our case) by a square-well potential with depth ϵ , and variable range, λ . The number of segments, m , in the model chain does not coincide exactly with the number of carbon atoms, n , but follows a simple empirical relation: $m = 1 + (n - 1)/3$. Ethane is thus modelled by 1.33 segments, butane by two, etc.; and xenon is modelled by a single sphere.

The first striking feature of the intermolecular potential parameters (obtained, as usual, from fittings to the experimental vapour pressures and orthobaric densities), is the constancy

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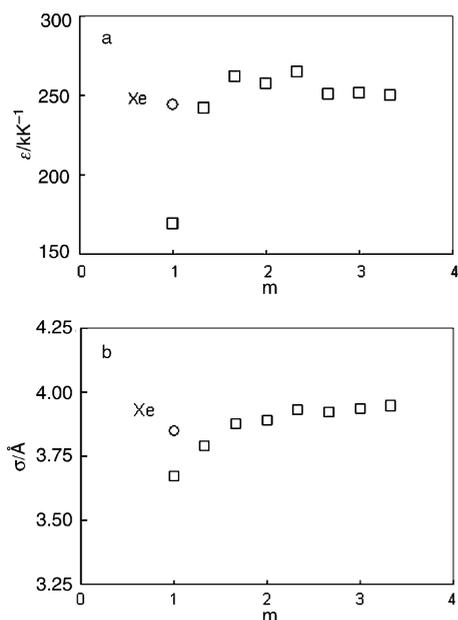


Fig. 1 (a) Intermolecular potential depth parameter, ϵ , and (b) segment diameter, σ , as obtained from the SAFT-VR theory for xenon (circle) and the n -alkanes (squares), as a function of the number of spherical segments, m , used to model the chain molecule.

of the depth of the potential, ϵ , for these short alkanes (Fig. 1a). (Methane is a known exception,¹⁶ but xenon fits in with the other n -alkanes.) As for the diameter, σ , which increases with chain length, it can be seen from Fig. 1b that the value for xenon follows the trend of the higher hydrocarbons. (The range parameter, λ , increases slightly throughout the series, but once again the value for xenon is that of a typical n -alkane.) It appears from the SAFT-VR parameters that xenon belongs with the n -alkane series, behaving more regularly than the first terms of the series, methane and ethane. Average values for the higher n -alkane (propane – n -octane) parameters are (0.391 ± 0.004) nm for σ , and (256.0 ± 6.4) K for ϵ/k ; the corresponding values for xenon are 0.385 nm and 243.3 K, respectively. In other words, xenon can be modelled by a sphere with almost the same diameter and attractive energy as those used to describe the n -alkanes. It should be noted that the size of the xenon atom—measured, for instance, in terms of van der Waals radii—agrees well with that of the cross-section of the n -alkanes,¹⁷ (Fig. 2). These parameters have been successfully used to reproduce the experimental phase diagrams and the excess molar volumes of a variety of mixtures involving xenon, n -alkanes and other components.

The similarity between xenon and the n -alkanes extends to other types of properties. Second virial coefficients, for instance, are insensitive to the individual values of the parameters, provided that their product, $\epsilon\lambda$, remains constant.¹⁸ (This reflects the importance of both size and polarizability in the characterisation of the well of the potential.) The values of $\epsilon\lambda$ correlate well with n (or m) for xenon and the higher ($n > 2$) n -alkanes. Likewise, the dielectric polarizability of

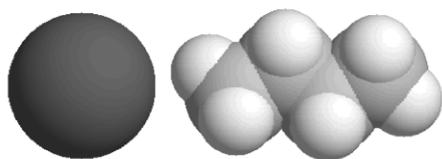


Fig. 2 Visualization of xenon and an n -alkane (n -butane) molecules according with the van der Waals radii.

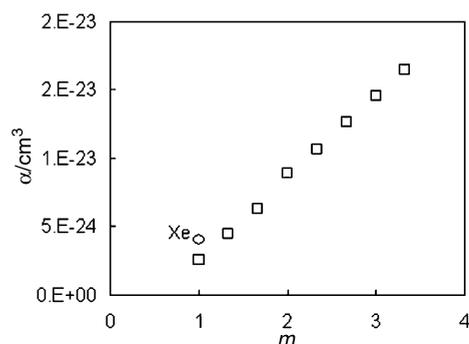


Fig. 3 Dielectric polarisability, α , for xenon and the n -alkanes as a function of the number of spherical segments, m .

xenon fits well with the linear dependence on n exhibited by this property for the n -alkanes,¹⁹ as seen in Fig. 3.

Macroscopic properties

Several thermodynamic properties have been examined. In Fig. 4, for instance, the critical pressures, p_c , for xenon and the n -alkanes are represented against the number of spherical segments, m (as previously defined). As before, xenon follows the trend of the higher hydrocarbons. Similar conclusions could be inferred from plots for the critical temperature, T_c , and (although less clearly) the critical volume, V_c .

Molar enthalpies of vaporization, ΔH_{vap} , and the Hildebrand's solubility parameter,²⁰ δ , provide another instance of the similarity of behaviour between xenon and the n -alkanes. The Hildebrand's solubility parameter is effectively a measure of the cohesive energy density of the liquid and can be related to ΔH_{vap} , as $\delta = [(\Delta H_{\text{vap}} - RT)/V_m]^{1/2}$ where R is the gas constant, T the temperature and V_m the molar volume. Plots of either ΔH_{vap} or δ for the noble gases and the n -alkanes, against the number of spherical segments, m , show that xenon fits the n -alkane correlation, whereas methane does not (Fig. 5).

Finally, transport properties have also been addressed. In this case however, no correlation could be observed between the behaviour of xenon and that of the n -alkanes.

Extension to anaesthesia

Led by this structural analogy between xenon and the n -alkanes we have searched for further confirmation of the observed behaviour in other fields, such as that of anaesthesia.

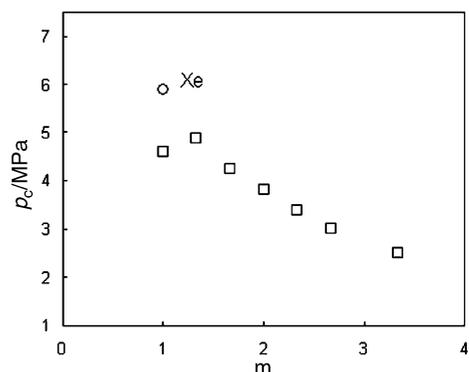


Fig. 4 Critical pressures, p_c , for xenon and the n -alkanes as a function of the number of spherical segments, m .

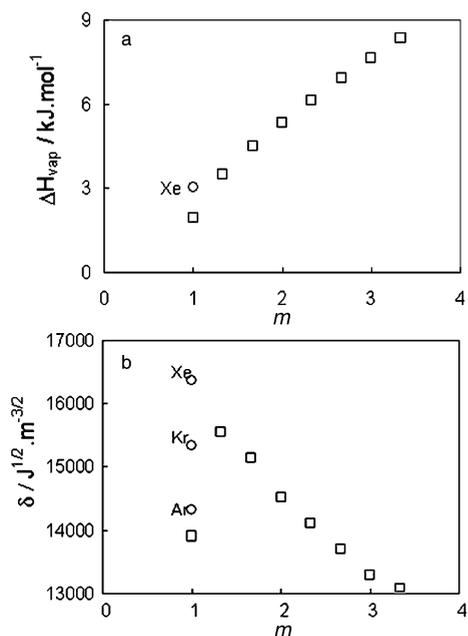


Fig. 5 (a) Molar enthalpy of vaporization, ΔH_{vap} , and (b) Hildebrand solubility parameter, δ , for the noble gases (circles) and the n -alkanes (squares), as a function of the number of spherical segments, m , in the molecule.

The anaesthetic properties of xenon were first studied by Cullen and co-workers²¹ and since then this question intrigues the scientific community. Given its chemical inertia, non-toxicity and non-flammability, which make it an easy and safe gas to handle, xenon has become a very desirable anaesthetic and very recently, its use has been submitted for regulatory medical approval in Europe.²²

The molecular mechanism of anaesthesia has been widely researched in the last decades but still remains unknown.²³ Argon and krypton also have anaesthetic properties but only xenon is an anaesthetic under normal pressure conditions.

Liu *et al.* have studied the anaesthetic properties of the n -alkanes in rats²⁴ as well as their solubility in blood,²⁵ saline and a number of lipids.²⁶ More recently they have performed similar experiments with the rare gases, including xenon.²⁷ Using these results we have compared the anaesthetic properties of the two families.

In Fig. 6, the anaesthetic power of the heavier noble gases and of several n -alkanes measured as the minimum alveolar anaesthetic concentration (MAC),^{25,27} as well as their blood/

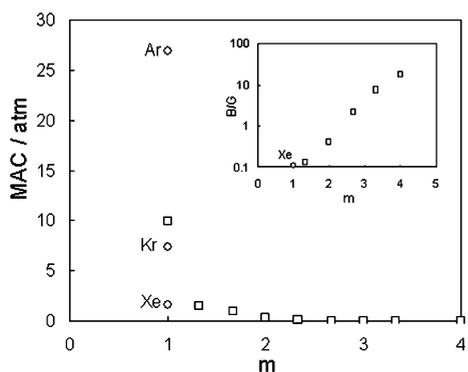


Fig. 6 Minimum alveolar anaesthetic concentration, MAC, for the noble gases (circles) and the n -alkanes (squares), as a function of the number of segments, m , in the chain molecule. The inset shows the blood/gas partition coefficient, B/G, for xenon (circle) and the n -alkanes (squares), as a function of the number of segments, m .

gas partition coefficient (B/G),^{25,28} are plotted as a function of the number of spherical segments. As can be seen, whereas methane is an exception, xenon follows the general behaviour of n -alkanes.

According to Franks and co-workers²⁹ it is probable that anaesthetics act directly on proteins rather than perturbing lipid bilayers. Moreover, there is experimental evidence for believing that the anaesthetic site should be a predominantly hydrophobic “pocket” with well-defined dimensions.³⁰ As for the forces involved between the anaesthetic molecule and pocket, there is generalised agreement that these should be London dispersion forces.²³ Very recently, Quillin and co-workers³¹ explained the binding of noble gases within apolar cavities of proteins, in terms of size and polarizability of the ligand molecules. In this context it should be noted that xenon, like many of the n -alkanes, can also form stable host–guest complexes with a number of host molecules, including cryptophanes³² and hemicarcerands.³³ We believe that the exploration of the analogy now reported may contribute to a better understanding of the mechanism of anaesthesia at the molecular level.

In conclusion, the underlying feature to all these analogies is the similarity of repulsive (size) and attractive (dispersion) energy between xenon and the n -alkane units. It is this double coincidence that points to xenon as an “ennobled n -alkane”, the first member of the series.

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