SUPPLEMENTARY INFORMATION added to the proofs

Reports of Referees A, D, and H (received 13/12/2023), and responses and changes (in italics) provided by the Author to the Editor (18/12/2023).

General remarks from the author to the editor on the referees reports:

Dear Editor, cher Pierre,

The Referees' reports are, to say the least, unexpected but enlightening, and my paper must have been just as unusual and surprising, even unsettling (I don't dare say innovative) for the Referees.

It is amazing to note the magnitude of the differences in opinion expressed by readers known to and selected by the author, and by anonymous readers/referees recruited by the Editor.

None of the Referees noticed any scientific error. The question raised by **A** was actually answered in-depth and duly illustrated in both this paper and in Angew. It is very curious that he raised it (and in a rather incomplete way).

No doubt that the standing of the Referees chosen by the Editor is such, bigwigs certainly, that they cannot imagine that less gifted people could, for example, misunderstand the implications of the « cage » denomination, or ignore that a granted patent could impress a layperson, even a chemist or an editor, and fool examiners from patent offices.

Altogether, **A** focalizes excessively on one issue, and laughs at it (which is ok). His only scientific question *was* actually extensively discussed without him noticing it! **D** reveals disputable ethics and an undisputable inclination for censorship. **H** quibbles, provides marginal yet sometimes useful suggestions, and plays dumb whenever he can.

Finally, and most alarmingly, none of the three Referees appears to care the least about commonplace didactic questions, correcting science when needed, impending scientific publishing issues, and even less about societal issues. Luminaries have better things to do.

Referee A, remarkably, left the decision to publish or reject the paper to its author. Here is his report:

The author is a superb chemist, a master of organic fluorine chemistry. He is much incensed at the treatment he has received from stupid reviewers and silly reviews of his excellent work on fluorinated polyhedral compounds in the literature. And similar absurdities in the patent literature. On receiving such reviews and seeing these crazy patents, most people would imbibe a glass of a single malt whiskey, curse the reviewers in a variety of languages, and go on.

I am sure that the author's patents never exaggerate, but any good chemist knows that the patent literature is replete with unphysical claims and reactions that are not reproducible. Ditto for Wikipedia. Dr. Riess instead goes on, at great length, to the extent that he falls to this reviewer in the land between the wonderful line in the classic "Casablanca" film, where Claude Rains, as Captain Louis Renault, says "I'm shocked, shocked that gambling is going on in here", and the turn of phrase that has entered common English parlance, derived from Gertrud's statement in Hamlet Act III, "The lady doth protest too much, methinks". I bet there is a like expression in French, as the tendency to go on

in criticism is there in every culture.

The author criticizes quite correctly what he sees from his stupid critics, at some length, but misses the opportunity to instruct by asking the question: How big a cage do you have to have in order to indeed get something inside? Experimentally, the answers are there: you can get He or N atoms and H_2 , and even a water molecule inside a fullerene. A silsesquioxane [$Si_8O_{12}R_8$], pretty close o a saturated hydrocarbon ele ctronically, will (for some R) bind a fluoride ion inside it by 70 kcal/mol. Aside from the verbosity, there is nothing wrong or wrongly reasoned in this paper. It does fall within the Opinion Piece rubric. Publishing it will occasion amusement for the reader, because of the absurdity of the opinions and patent mistakes Dr. Reiss details. Even though he is correct in his views, Dr. Reiss would be advised to NOT publish the essay – it will make the readers smile as much at him than at the fallacious behavior he delights in detailing.

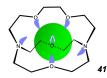
Author's comments: The undoubtedly illustrious and respectable Referee A is absolutely right: why bother with censorship in scientific journals, correct wrong notions, expose absurd claims and fraudulent patents, care about naïve investors being deceived, or bother about any issues currently faced by scientific edition? Top scientists should not waste their time and worry about such petty issues. The Illustrious Referee would obviously never make the mistakes that many humbler chemists actually do (see ref [2]).

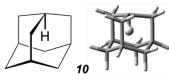
Referee A focuses (over one-half of his report), with welcome humor, on the author's troubles with the Editors of Angewandte, which he wants to perceive as the paper's finality while it is only a practical pretext, of little importance indeed (lines 489-490 said "Whether or not the paragraph about perplexing patent EP 0 261 802 B1 was comprised in our review about perfluoropolyhedrane is of little consequence.") that the author used to express his opinions on plentiful other teaching, publishing, patenting, and editing issues.

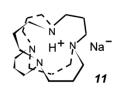
I tried to smooth and reduce the Angew censorship "affair". A few lines were removed. In the abstract, I added a line mentioning other topics of interest.

The only, truly scientific question raised by the Referee, namely "How big a cage should be in order to get something inside?" **WAS** actually discussed in detail, both in the present paper and in the Angewandte review (ref [2]). Not only the size of the "cage" but also the size of the apertures, the conformational flexibility of the frame, and the presence of donor atoms, which means both thermodynamic and kinetic aspects were considered. In the present paper, see lines 141-144 and 257-260; Footnote 1; Ref 19 and 36; and Structure **11** in Fig. 6; and Graphical Abstract. In Angew. Chem., see page 11, 2^{nd} column last five lines; structure **40** versus **41** in Fig. 12; ref. 107). The case of fullerenes was also duly reviewed in [2] Sections **2**.2.5, **4**.1, **4**.3, **5**, **6**.3, and **7**; "fullerene" is mentioned 18 times. In this paper, see lines 178-180 about O_2 in C_{60} and ref. [25]. How could Referee A miss all this??









But chemists can also (unpretentiously) try to behave as responsible citizens, express doubts*, expose misconceptions, denounce fraudulent claims, care about scientific publishing issues, counter inbred thinking, favor human exchanges, etc. Are these not serious matters? Should there be a barrier between Science and Society? No impact? And the author would feel rewarded if some of the absurdities and mishaps he exposes could also cheer up a few Readers.** Other Readers may, hopefully, feel concerned with some other issues like accepting or not censorship, agree or disagree with some of the multiple opinions that are offered, and (hopefully) find here some food for thought and further discussions.

^{*«}Of all [science's] many values, the greatest must be the freedom to doubt» R. Feynman 1955.

^{**} As it stands, only one of the three Referees smiled, unfortunately.

Referee D recommended the rejection of the paper:

This paper makes the point that small molecular cages cannot reasonably be expected to contain anything. While I'm sure that this assessment is correct, it appears blindingly obvious that a cage must be significantly larger than the thing encapsulated. It is also quite clear that the patent literature contains a great deal of bad science. I'm therefore not sure who would benefit from reading this work.

Author's reaction: I am not sure that the Referee has read much of the papers (Angew. review + CR opinion). In any case, he only mentions two of the issues that are developed. The literature (ref [2]) tells us that what is obvious for him is not for many less bright colleagues, students, patent lawyers, patent examiners, editors, etc. Concerning patents, He knows that they can contain bad science, but does not care about any consequences. He fails to address the many other issues and opinions discussed in the paper.

Clearly, this Referee is not interested in any of the subjects addressed in this paper, which is his right, but disqualifies him as a referee.

Consequently, he should have declined the invitation to review it.

Instead, by rejecting the paper, he decided that no one else, including you my Reader, should be interested.

Referee H found the paper acceptable after major revision.

Author's comments are given *in italics* directly on the Referee's report sheet.

This is a strange (say unusual, yes) piece, because there are two (at least four interrelated) topics (and many more sub-topics) in one article:

- -one about the "impossibility" of hosting O_2 (or any other atom, ion, or molecule) in some "cage compounds"
- the other about the behavior of the editors of Angewandte Chemie (and, more broadly, censorship and publication ethics in general).

But also

- an illustration of absurd claims taken from the patent literature, and their consequences.
- many general considerations and opinions about present-day scientific publication and editing issues that may provide food for thought and foster useful discussions.

By the way, this what should be announced in the title/abstract/introduction. The items mentioned by the Referee were announced in the title and/or abstract, and introduction. I now added one more line in the abstract about items the Referee did not mention.

The authors are chemically competent, and I did not see scientific mistakes, even if I were more cautious than they were about the so called "impossibilities": the history of chemistry showed many cases in which the impossible occurred (think of the discussion on quantum physics, quantum intrication and velocity of light, tunnel effect, etc.). Yet there seems to be a consensus that velocities larger than that of light, or perpetual motion may be impossible. Or, to the best of our understanding, that a grown chicken could hardly be hosted in a normal chicken egg.

At its first occurrence (line 296) the word impossible was qualified as follows: "dimensional characteristics of guest "cages" ... predict that hosting O_2 in **8** is, for all practical purposes, impossible". Is that not cautious enough?

Now, the text is somehow redundant, and it would deserve trimming. In particular, repetitions should be avoided.

I have tried my best and cut out some 28 lines (but added some more on other topics), although teaching in some cases requires repetition, especially when the angle of approach is changed.

And many references are missing, to establish some points. Such texts should be less rhetoric, and more referenced. This is discussed point by point thereafter.

Finally, the authors should not confuse a reduction ad absurdum, a precise way of reasoning, and showing absurdities. I clearly did both, reasoning and confronting with the absurd. The question of what a "demonstration by the absurd" is, and the meaning of "absurd" is recurrent in the Referee's observations, and is dealt with here.

I define "absurd" lines 106-107 by synonyms provided by standard respectable dictionaries. Line 108 I proposed "a form of refutation". The premise of my reasoning is the presupposition that a "cage compound" should be able to encage such or such atom or molecule; this supposes that the space available in the cage is comparable or larger than that of the item to be encaged; the presupposition is contradicted by the comparison of known atomic and van der Waals radii, which shows that this is not the case; which means that the presupposition was absurd. In other words, if you nevertheless try, following Socrates' invitation, to force the latter in the former, our extrapolated knowledge about dodecahedrane, for example, tells us that the former, if it could be formed, will tend to blow in your face with the utmost energy. And Britannica adds: "In common speech the term reductio ad absurdum refers to anything pushed to absurd extremes." I now include this in the text, with the Britannica as a reference. I also use "refutation" and "confrontation with the absurd" when appropriate.

The Referee should tell in which way Daigle's Master thesis, which argues that Aristoteles was not the first to use reductio ad absurdum reasoning, is relevant.

And many details have to be fixed.

Thanks for the numerous questions and suggestions. All the Referee's observations and rhetorics have been given due consideration as indicated below.

I propose publishing the text after a revision.

Detailed observations:

L3-11: It is not a demonstration by the absurd, but only a refutation of a proposed idea. *Please see above discussion*.

The title is too long, too many ideas. Why too long? In my opinion, a title should inform about the content. And yes, there are many ideas. Too many?

19: Who said that cubane is a cage compound? For example, the paper co-signed by Philip Eaton, the first chemist to have synthesized cubane: "X-ray structures of cubylcubane and 2-tert-butylcubylcubane: short <u>cage-cage</u> bonds". J. Am. Chem. Soc. **110** (21): 7232 (1988). More recently, the inventors of perfluorocubane designate it as a "cage-compound" in M. Sugiyama, M. Akiyama, et al., Science, **377** 756-759 (2022); (ref [8]).

See also: "On the Viability of Small Endohedral Hydrocarbon Cage Complexes: X@C4H4, X@C8H8, X@C8H14, X@C10H16, X@C12H12, and $X@C_{16}H_{16}$ by Damian Moran, H. Lee Woodcock, Zhongfang Chen, Henry F. Schaefer III, and Paul v. R. Schleyer*, J. Am. Chem. Soc. **125**: 11442 (2003). See further references in [2], to which I now added the customary (but useless) "and references therein".

46. There is no need to answer this question, because the answer is yes: there can be non covalent associations between polyhedranes and other compounds... outside them. See Lehn, Supramolecular chemistry, concepts and perspectives. This remark is so obviously irrelevant: the question raised throughout the paper and in Ref [2] unambiguously concerns the use of polyhedranes as host

compounds. Can one put anything <u>inside</u> the "cage"? The paper's title specifies "<u>lodging</u> capacity". The sub-title in line 46 is immediately qualified in the 1st paragraph, which reminds us that we are examining the polyhedrane's "<u>hosting</u> capacity". The 2nd paragraph contests the belief that they could easily "<u>host</u>" atoms, etc. How many more times should it be repeated? And the Referee complains about redundancies....

- 47-51: the author would be clearer if he made two sentences. OK, there are now two sentences.
- 47: italics for Ang Chem; OK, I have put it in italics
- 52: no capital at Researchers; OK, I removed the esteeming capital.
- 53: it is ambiguous. Did [3] write that cubane is a "cage compound"? Sorry, I don't have the book. I borrowed mine but had to send it back. But some examples are provided above for line 19. Note also that Olah's edited book was dedicated to and included a paper by Paul von Ragué Schleyer who definitely includes cubane in his studies of "cage compounds".
- 55: do you think really that looking at these pictures is enough to admit a cage property? Some obviously do (please see ref. [2]), especially when they are called "cages", and not only in patents.
- 55-58: please give them, as critics should be precise. This is documented and discussed at length in ref [2], the content of which cannot be plagiarized here but is cited just three lines earlier.
- 86 : at this step, we don't know where we go. ?? Please read the next lines (86-91), which precisely introduce Sections 2 and 3.
- 86 This is not a demonstration by the absurd, but simply the observation that it is absurd to imagine that some "cage compounds" are indeed hosting other species.

 See https://www.britannica.com/topic/reductio-ad-absurdum and Daigle, 1991
 (https://scholarworks.sjsu.edu/cgi/viewcontent.cgi?referer=https://en.wikipedia.org/&httpsredir=1&articl

Please see the earlier general comments.

<u>e=1228&context=etd_theses</u>)

- 87: comparison rather than inspection (because of versus) Agree and changed it.
- 88: the parenthesis is useless, and it blurrs (*rather explains*) the question. More generally, the authors would make a stronger argument if they would "clean", "trim" their manuscripts. All what is not strictly necessary for the demonstration is weakening it. *The Referee would have written it in his way, and probably for a more restricted public.*
- 89 : please give the references to the patents *They are unambiguously designed by their US Patent Number in Section 3 where they are discussed, as well as in the caption of Figure 3 at the end of the sentence.*

106 and subs: this is not the right definition of demonstration by the absurd See https://www.britannica.com/topic/reductio-ad-absurdum and Daigle, 1991 (https://scholarworks.sjsu.edu/cgi/viewcontent.cgi?referer=https://en.wikipedia.org/&httpsredir=1&article=1228&context=etd_theses) This question has been addressed earlier.

109: no, lay people don't even know this demonstration (prove it). Show me an example. In my opinion lay people are not necessarily idiots.

And references are missing for this this part. Are references really needed here?

- 109-111: vague, no reference. Same.
- 112: reference missing. And again this is not a demonstration by the absurd. Who says it is? A reference ([16]) is now added.
- 112: scientific papers should not repeat what was already published elsewhere, and instead a reference is to be given. What is the Referee talking about?? See lines 55-58.
- 112: not only of teaching, but also of having political discussions. *True. I added the political element to the sentence.*
- 113. This is not <u>exactly</u> true. Often, Socrate (as depicted by Plato) considers only commonsense ideas and by a game of skilled deductions it(?) arrives to the contrary of what the person wants to express. See earlier discussion.

And sometimes (Theetete, for example) there is nothing to do with refutation, but only to make people say what they "don't know". *In this paper it is definitely about refutation.*

- 114. Confrontation with the absurd is not the same as demonstration by the absurd. Agree.
- 115: vague, no reference, no demonstration A clear opinion that requires none! Do opinions necessarily need to be a rehash of some already expressed ones?
- 117: No, see below. ??
- 119: what is meant by "etc."? References? Etc. etc. is used at the end of a list to show that you have not given a full list. etc is a written abbreviation for `etcetera' (Collins Dictionary).
- 121 : do chemists eliminat absurd propositions, or simply wrong possibilities/hypotheses? *I replaced propositions by possibilities/hypotheses but do not see what is wrong with propositions.*"unconscious": no, we are perfectly conscious, otherwise silly. *Agree, unaware or automatic would be better. But I suppressed the whole sentence.*Reference? *Just a personal opinion.*
- 133 : seldom : do you have statistics? Does the Referee have any on the contrary?
- 138 : about sizeable number, how much? references ? *Reference (2) at the end of the sentence provides a fair number of examples and references. Please read.*
- 140: this concept should be cleared with precision. For example, one can measure the residence time "inside" a phospholipid micelle by electronic paramagnetic resonance, and it is not nil (Bezuglaya et al, 2022) What precisely is the Referee's point?
- 144: are footnotes accepted by the journal? Personnally I consider that they should not be present, because either the information given is needed for the understanding of the text (and they should be in the text), or they are additions (and they should be dropped). Footnotes have many virtues: they can provide supplementary information, commentaries, clarifications, citations, and elaborations on ideas without disrupting the flow of the main text; they allow ancillary considerations, including warnings, or far-fetched, but possibly inspiring thoughts or associations; and for some reasons, footnotes can attract the Reader's attention and highlight some thought, developments, and complexities. Footnotes sometimes also offer some sort of aside (en apparté) communication with the Reader. And why should one renounce using footnotes? They provide a recognized, formalized tool in academic writing.

145: a wealth: how much? Only one reference [20] to give them all? The reference provided is [2] and references therein, which review them. Please see.

148-154: and what about quantum effects? The Referee should look up the references provided in [2]. The present paper cannot and does not intend to repeat/plagiarize [2].

152-155 : reference missing. This sentence and the preceding one summarize the content of ref [20], which has just been cited line 148.

156 : drop (one He atom within a $C_{10}H_{16}$ frame), as it is obvious in the formula before. The parenthesis is needed as it defines the meaning of the @ notation, which is used here for the first time.

156 and others: the units are not given correctly, write: kJ.mol^-1 (here, I cannot pub the -1 in exponent, and this is why I am using ^). Sorry, but the kJ mole⁻¹ writing follows the IUPAC rules (see the Green Book).

159. And what about having only one O atom of O_2 ? Here we are not concerned with O, but specifically with O_2 , dioxygen.

160 : little, but how much? reference? Little is now replaced by a prudent "no evidence the author knows of".

190: is it a confrontation, or simply a comparison? *Confrontation seems fine for me, but OK for comparison*.

192: again about footnotes Same diverging opinion about footnotes as for line 144.

209: personnally, I would be more cautious, because the history of chemistry amply demonstrates that "impossibilities" were not impossible! *Am I not cautious enough by saying: "At this point, one can safely conclude..."?*

214: what is life-saving doing here? Is it not a vital characteristic of O_2 ? The importance of this point was hinted at line 89 and will become obvious in the following Section.

231: I would hesitate about this "without any doubt" I now deleted "without any doubt", not because one could have some doubt, but because the experimental data do not leave any doubt about the absence, by far, of space for lodging O_2 inside that compound.

235 and 238: again, about the demonstration by absurd, it does not mean being absurd, but contradicting facts, from an hypothesis that is refuted ipso facto. *See earlier comments*.

240: the authors repeat themselves, and this does NOT make the point stronger, on the contrary. Moreover, scientific literature should be concise. *Well, didactics sometimes require repetitions.*

241: what could be a non ordinary chemist? *Now replaced by average.*

245: not sure that it is useful to translate Pa in atm. The readers of this journal can do that by themselves, if needed. *No doubt, but I just took the GPAs out*.

247: it is the second time that oxygen is considered for applications. Do the patents consider this question? If yes, it would be good to say it much before, when the patents are first considered. *I agree and added it on line ex-91.*

258: footnote, see above; see opinion about footnotes as for line 144.

275 : no capital for inventors (also later). For emphasis and easy identification of specific Inventors.

296 : idem. Idem.

297: already said. Here we criticize for the first time the Inventors' approach.

299: already said in 293. 293 is about O_2 dissolving capacity, while 299 is about O_2 transport capacity, which is not the same, as only the second involves kinetics; this was explained in lines 449-50.

318: what does "...." mean? Ellipses, a recognized punctuation symbol here expresses stupefaction, incomprehension,... Ellipses also lets the Reader introduce his own words after having pondered the information. An exclamation point (!) would essentially convey the same but in a more abrupt way.

319-321: this is rhetoric, and it weakens the idea. The Referee's opinion, not mine.

324: no capital to "contradictor", and it would suffice to say "referee" *I do mean Contradictor and want to highlight it. A referee is not necessarily a contradictor. It is also a way to identify this specific participant for later use.*

326: "resented our mention of a Google search" is not clear. Please explain why?

327 : no capital to readers. *Again, a way to distinguish an essential and respectable class of individuals.*

330. Here there is a very important question: if the authors discuss a paper in another journal, they should probably write a Letter to the Editor in this journal. It could indeed be a possibility, among others, in specific cases. It is not appropriate to discuss multiple issues, with Tables, multiple Figures, structures, and references. Accessorily, Angew. does not feature Letters to the Editor.

332: not sure to agree; it is only a demonstration that patent can be given even when the invention is nil (imperfection of all humain enterprises) We are talking about specific patents that support our point. And I think that imperfections, here absurdities, can/should be exposed, discussed, and corrected.

338: this is well known, isn't it? *Apparently not to some Referees, students, average chemists, or the naïve investors...And what about patent Examiners?*

342 : no capital to referee. It concerns a specific Referee: for emphasis and identification again.

342: write "The referee did not criticize our writing because what we wrote was wrong, but because it was "badly written" *I now use the Referee's proposition*.

356: here I would certainly drop the footnote for the reason given before, but ALSO because the humour is out of place. The authors should not be personal. Facts, only facts. *Really, facts alone?* Without critical scrutiny, skeptical assessment? Sure that you always have the right facts, all the facts needed for understanding an increasingly complex situation, environment, and their consequences, including, among others, human and societal? No debatable uncertainties ever? No room for doubt (see new Footnote 12), opinions, controversies, human exchanges, and style in science? At the risk of

further isolating science from society? And ALSO because Scientific Journals must be humorless, boring, and dehumanized?

360 : "one Contradictor": is this the former referee? *Yes, the text said "that one Contradictor" and now "the above cited Contradictor"?*

362: write "instead of the French guillemets" Done.

432 : why You with capital? Why not, for emphasis and directly addressing the Reader?

454: Indeed, if I were the Editors, I would say that it is an issue of article kind. A review is NOT a Letter to the Editor. And the Ang Chem from the authors was a "review". It remains to see the editorial rules of the journal. No opinions allowed in Reviews? And should patents be excluded from discussion in reviews? Angewandte's Instructions say: "Rather than an assembly of detailed information with a complete literature survey, a critically selected treatment of the material is desired; unsolved problems and possible developments should also be discussed".

Personnally, I am not hurt by their decision, but I feel that they could have invited the authors to make a separate paper on this. A matter of opinion...and acceptance/approval of censorship.

From here on, the authors repeat and repeat the same ideas. *And many new ones*. I would advocate to be more concise as the readers understand well the issue. In particular, the lines 474-476 should be dropped. *Expressing the rights of Authors (lines 472-474) is ok, but not those of the Reader?*

Lines 490 and subs: this could be much reduced. The authors "overflow". *No, he expand, considers further related issues, and offers additional personal opinions.*

503 : references are missing. The paragraph provides personal opinions, not some rehash of published materials. Hopefully, many other individuals are concerned with these issues and express similar and other views and in many places.

After 510: this is another topic. *Indeed, this Section provides an expansion to multiple interrelated considerations and opinions.* And the authors, who speak of "verbose", could be more concise. *Well, try to mention some 22 (semi-colon-separated) distinct debatable issues in 37 lines, little more than one standard page. The Referee could have highlighted the less troubling ones and recommended removal.*

I modified the sub-title to better reflect the content. However, the Referee does not seem much interested in the future of scientific publication and editing. I hope that I am wrong on this point. About verbosity: I have noticed that usage of academic English and of somewhat infrequently used but better-fitting words are often happily mistaken for verbosity.