THE JOURNAL OF PHYSICAL CHEMISTRY

Article

Subscriber access provided by UNIVERSITY OF ADELAIDE LIBRARIES

ADELAIDE

N in Solution: Isotopic Labeling and Further Details of its Synthesis by Phenyl Pentazole Reduction

Boris Bazanov, Uzi Geiger, Dan Grinstein, Shmuel Welner, and Yehuda Haas

J. Phys. Chem. A, Just Accepted Manuscript • DOI: 10.1021/acs.jpca.7b04222 • Publication Date (Web): 15 Aug 2017

Downloaded from http://pubs.acs.org on August 18, 2017

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a free service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are accessible to all readers and citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.



The Journal of Physical Chemistry A is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

N₅⁻ in Solution: Isotopic Labeling and Further Details of its Synthesis by Phenyl Pentazole Reduction.

Authors: Boris Bazanov, Uzi Geiger*, Dan Grinstein, Shmuel Welner, Yehuda Haas⁺.

<u>Affiliation</u>

B. Bazanov, U.Geiger^{*}, D. Grinstein, S. Welner, Y. Haas:

Institute of Chemistry, Safra Campus

The Hebrew University of Jerusalem

9190401 Jerusalem (Israel)

E-mail: <u>uzi.geiger@mail.huji.ac.il</u>

phone: +972-54-5279783

+ - deceased

Abstract

The cyclopentazolate anion, N₅⁻, has been researched extensively over the years and detected in the gas phase more than a decade ago, but was only recently measured in solution. The process whereby aryl pentazole reduction leads to the production of N₅⁻ is still not fully understood. Here, the production of N₅⁻ in solution was investigated using isotopic labeling techniques while implementing changes to the synthesis methodologies. ¹⁵N labeled phenyl pentazole produced appropriately labeled phenyl pentazole radical anions and N₅⁻ which, upon collision induced dissociation, produced the expected N₃⁻ signals. Changing to higher purity solvent and less coated Na metal allowed for a much more rapid pace, with experiments taking less time. However, the best yields were obtained with heavily coated metal and much longer reaction times. Utilization of a vacuum line and ultra-pure solvents led to no products being detected, indicating the importance of a sodium passivation layer in this reaction and the possibility that sodium is too strong a reducer. These findings can lead to better production methods of N₅⁻ and also explain past failures in implementing aryl pentazole reduction

Introduction

The first successful synthesis and identification of the pentazolate anion (N_5^-) in solution was published several months ago in a succinct and introductory manner.¹ In this paper we aim to elaborate on the synthesis of the N_5^- species, present more proof for its successful identification, and report on some of the intriguing results that were accumulated since.

Ever since the synthesis of aryl pentazoles in the late 1950's by Ugi and Huisgen^{2,3}, attempts were made to cleave the C—N bond of these compounds and produce the pentazolate anion. A major push to these experiments was made when N_5^- was identified in the gas phase by collision induced dissociation of para oxidophenyl pentazole⁴ and then by laser desorption ionization of para dimethylaminophenyl pentazole⁵. Yet, all past attempts of attaining the same result in condensed phases by reductive, oxidative and photo- cleavage methods have failed.^{6–} ¹¹ Two possible exceptions are the CAN dearylation of para methoxyphenyl pentazole yielding N_3^- which is probably a decomposition product of N_5^- , ^{12–15} and more recently, the detection of a solid pentazolate salt by oxidative cleavage of 3,5-dimethyl,4-hydroxyphenyl pentazole¹⁶ which could be further converted into cobalt complex ¹⁷.

An in-depth computational investigation of the link between the aryl pentazole radical anion and the formation of N_5^- in one of the gas phase experiments provided an indication that it should also be present in solution.¹⁸ This led to the first experimental detection of the phenyl pentazole radical anion (PPRA) and N_5^- in solution.¹ Due to the brevity of the initial publication, some key aspects were not included in the report of this discovery, including identification proof by means of isotopic labeling and MS/MS techniques. Further progress has also been made since the initial discovery, including changes to the synthesis method and observations regarding its successful application, warranting this report. Regarding the latter, we have observed a key parameter affecting the outcome of the procedure that may lead to serious issues with reproducibility of results if left unknown to the community.

Experimental

<u>Warning!</u> Phenyl pentazole is a sensitive explosive prone to detonation upon warming to <u>room temperature.</u> N_5^- , its salts, and compounds are expected to be both sensitive and <u>powerful explosives.</u> All precautions should be used when dealing with such materials.

Materials and instruments

Tetrahydrofuran (THF, Analytical, Frutarom LTD. or anhydrous, Sigma Aldrich) was either dried over activated A4 molecular sieves (Sigma) for at least 48 hours or refluxed over sodium (Aldrich, \geq 99.8% trace metal analysis) and benzophenone (Sigma, ReagentPlus, 99%) for at least an hour under an atmosphere of nitrogen in a solvent still before use. Sodium metal (Aldrich, cube in mineral oil, 99.9%) was cut under isooctane (Fluka, for UV spectroscopy) and wiped from excess solvent before use. Aniline (Sigma-Aldrich, ACS reagent, \geq 99.5%), sodium nitrite (Aldrich, 95%), sodium azide (Sigma, ReagentPlus, \geq 99.5%), hydrochloric acid (ACS reagent, 37%), methanol (Biolab, HPLC grade, \geq 99.9%), and acetonitrile (Biolab, HPLC grade, \geq 99.9%) were used as received. ¹⁵N-labeled sodium nitrite, aniline, and sodium azide were obtained from Cambridge Isotope Laboratories Inc. and used analogously to the unlabeled materials.

MS data were recorded on an Agilent 6520 Accurate mass Q-TOF LC MS machine with either a C18 column or no chromatography at all (analogous to ESI-MS):

 μ L of the solution were immediately injected to a LC-MS using Hypersil BDS C18 column (particle size 5 μ m, length 100 mm, internal diameter 4.6 mm, #28105-104630) or only union (no column). The following gradient separation method (for on column separation) or isocratic one using 100% methanol as a mobile phase (for non-column method) was used:

Time (min)	Acetonitrile	Water
0	0	100
5	100	0
10	100	0
15	0	100

Analysis of the eluent was performed on an Agilent 6520 Accurate mass Q-TOF LC MS operating in the dual ESI negative ion mode using nitrogen as a drying gas. The LC-MS parameters were slightly modified from the standard ones:

Parameter	Standard	On column separation	Non-column
		experiment	experiment
Flow (mL/min)	0.5	0.5	0.25
Volume injected (µL)	3	10	10
Cooling of vile	No cooling	Vial cooled	Vial cooled
Vcap (V)	3500	3000	2500
Gas temp. (ºC)	350	300	350
Drying gas (L/min)	10	9	8
Nebulizer (psig)	40	35	35
Fragmentor (V)	150	50	100
Skimmer (V)	65	65	65
Octopole RF peak (V)	750	750	750
Collision energy	0	0	10

Preparation for LC-MS analysis included the transfer of solutions to 2 mL HPLC vials while taking care not to transport sodium pieces together with it. The vials were either kept cold with dry ice on the auto-sampler or allowed to warm up to room temperature for other experiments. No special care was taken to exclude air from the sample vials at this stage. It is noted that the total ion count signal peak for the methanol isocratic method started at 0.15-0.2 min and usually the baseline values were regained after roughly 1 min. The signal between 0.25 and 0.75 min was therefore averaged to yield a better S/N ratio.

A pure THF spectrum was measured the same way and used as background by subtraction from all spectra.

MS/MS was performed with different collision energies and an ion selector bandpass with 1.3 m/z FWHM.

Synthesis of regular and ¹⁵N labeled phenylpentazole (PP)

Phenyl pentazole was synthesized as before.¹ In a representative synthesis 1.86 g aniline, 4 mL hydrochloric acid, and 25 mL methanol were loaded into a beaker with a magnetic stirring bar. The beaker was immersed in an ice-water bath while stirring. 1.73 g sodium nitrite was dissolved in 10 mL water and added dropwise while monitoring and controlling the temperature of the solution at

0-5 °C. Following the addition step, the solution was allowed to stand in the bath for 30 minutes and then transferred to an acetonitrile-dry ice bath (-41 °C). 1.73 g sodium azide dissolved in 10 mL water was added dropwise while monitoring and maintaining the temperature below -35 °C. After azide addition the reaction was allowed 30 minutes to come to completion and the precipitated PP was collected by cold filtration at -30 °C in a sintered glass filter and washed with a cold (-20 °C) 50% water:methanol mixture. The solid product was collected into a small glass vial, which was placed on activated 5A molecular sieves (Sigma) in a big glass vial and stored at -78 °C. ~0.56 g (20.5% yield from aniline), ~90% purity with the rest being Phenyl azide by N.M.R. (¹H-N.M.R: 8.18 (D), 7.73 (M), ¹⁵N-N.M.R (tri-labeled, see below): 11.8 (D), -19.3 (M), -77.3 (M)).

The Journal of Physical Chemistry

Three types of ¹⁵N labeled PP were prepared by utilizing labeled aniline, sodium nitrite, and terminally labeled sodium azide. The incorporation of labeled reactants and their resulting isotopomers are summarized in scheme 1. It should be noticed that the tri-labeled material is actually a mixture of two isotopomers. The isotopically labeled PP is henceforth referred to as mono-labeled, bi-labeled, and tri-labeled, and the ¹⁴N material is henceforth referred to as unlabeled.



Scheme 1: ¹⁵N labeled reactant use and the labeling groups of PP used in this study.

Reduction of PP and liberation of N₅⁻

Method 1: About 1-3 mL THF, dried over molecular sieves, was placed in a small vial and cooled to (-40) – (-78) °C. PP was weighed into the vial to form a solution with approximate concentration of 0.01 M. A small piece of sodium was cut and washed with dry THF prior to being loaded into the vial. The reaction mixture stored at -40 °C for at least 2 weeks and at -78 °C for at most 3 months prior to separation of the solution from the metal and injection into the HPLC-MS. When needed, centrifugation was performed to receive clear solution. A chromatographic column was used in this method with a mobile phase gradient transitioning from H_2O to MeCN then again to H_2O , for five minute increments each.

Method 2: Distilled THF and sodium metal were loaded into a small vial. The vial was cooled to

-10 °C in a freezer and a weighed amount of PP was dissolved in it. Due to the need for speedy handling of PP, which may explode violently if left to warm to room temperature, the amount of PP varied between different vials. The metal was cut to smaller pieces, exposing a fresh metal surface, and the vial was left at -10 °C for an hour before the solvent was separated from the metal and the vial was taken out of the freezer. The best signals were usually obtained from samples left 2-2.5 hour at room temperature.

Method 3: Ace Glass Inc. glassware of the Airfree Schlenk type were used. THF was distilled from a sodium-benzophenone still to an evacuated Straus flask, from which it was distilled under vacuum when needed onto a sodium mirror in a 50 mL tube. Into a separate 50 mL tube solid PP was loaded and kept under vacuum at -20 °C for 15-30 min. THF was distilled onto it from the sodium mirror tube. Another sodium mirror was formed in a separate 50 mL tube, onto which the PP THF solution was transferred (under vacuum). The reaction was carried out for an hour at -10 °C in a freezer, after which the tube was vented and solution was drawn into an HPLC vial for further analysis.

Results and discussion

Strong MS signals at m/z=147 and 70 were observed upon HPLC-MS injection of a reduced PP in THF solution (according to method 1). These signals, with retention times of 7.9±0.7 and 1.9±0.4 min, respectively and are due to PPRA and N_5^- ions (figure 1A-D). When changing to mono-, di-, and tri-labeled PP, these signals shift, respectively, to m/z=148, 149, 150 for PPRA and to m/z=71, 72, 73 for N_5^- (figure 1E-J), all with the same retention times. Exemplary full range mass spectra at the two relevant retention times are presented in the supporting information (S1 and S2).



Figure 1: Chromatograms of the N_5^- signal at m/z=70 (A) and of the PPRA signal at m/z=147 (B). MS signals of the N_5^- (C, E, G, I) and PPRA (D, F, H, J) signals: from unlabeled (C, D), monolabeled (E, F), di-labeled (G, H), and tri-labeled (I, J) reduced PP solutions.

Method 1 for the reduction of PP produced signals of significant strength for PPRA and N_5 , but was flawed by long reaction times, large amounts of by-products from contaminant in the solvent, and inconsistent results (success rate of 50-70 % to our estimation). Method 2 was developed to overcome these drawbacks and incorporated better solvent purity and shorter reaction times at higher temperatures. The results of method 2 are much more consistent and can be easily reproduced. Despite its benefits, this method yields much weaker signals of N_5^- and no PPRA signals (these are assumed to be below noise levels). Change in the detection method accompanying reduction method 2 was intended to ameliorate some of these difficulties.

MS/MS measurements were performed on the N_5^- signal derived from differently labeled PP reduced using method 2 (figure 2). The only negative anion produced by collision induced dissociation of N_5^- is N_3^- with appropriate numbers of ¹⁵N atoms (scheme 2). This result supports the notion of a cyclic molecular species made up of symmetrically identical nitrogen atoms. However, it should be noted that if cyclo- N_5^- is produced at the cyclic configuration and later isomerizes to a chain form, the same results will be obtained – only direct structural data (15N-NMR, XRD) can fully elucidate the geometry of this molecular anion.



Figure 2: MS/MS signals from the N₅⁻ signal of un- (A), mono- (B), bi- (C), and tri- (D) labeled PP

solutions in THF reduced by method 2.





Scheme 2: dissociation of differently labeled cyclo- N_5^- to N_3^- ions, the theoretical ratio of product ions, and in parentheses the experimentally detected ratio of collision induced dissociation products.

Involvement of the solid electrolyte interface passivating the sodium metal was suspected, therefore an experiment using reduction method 2 and THF-d₈ was performed. Any negatively charged molecules produced directly from the solvent should have been easily spotted when compared to a control experiment. No such results were found, nor was any difference from the control results measured using regular THF. We can therefore conclude that no soluble anions were produced directly from the solvent and that the source of the passivation layer is probably contaminants such as gases (O_2 , CO_2) or products of the benzophenone-sodium reaction, which remain after a single distillation.

Reduction method 3 was initiated to better understand and control the parameters regulating the yields of the reaction. It yielded no detectable amounts of N_5^- in solution, but some N_3^- was detected in these solutions, unlike in the other methods. Warming to room temperature did not change these results. This finding, together with the lower yield of N_5^- of method 2 compared to method 1, leads us to conclude that sodium metal by itself is too strong a reducer and only the formation of a passivation layer (solid electrolyte interface, SEI)¹⁹ in the solvents of lesser purity facilitates the production of N_5^- . Such an outcome may indicate further reduction of PPRA to the dianion, which may then decompose to yield the azide anion. Past failures to produce N_5^- by aryl pentazole reduction are also explained by this finding – the reducing agent used, sodium in liquid ammonia,⁶ was too aggressive. It most probably prompted the production of the aryl pentazole dianion, which does not lead to N_5^- production. It also indicates a direction towards a quicker, cleaner production of N_5^- in solution by utilizing an intrinsically less aggressive reducer. Further research of this issue is currently underway.

Conclusions

Isotopically labeled N_5^- was produced in solution by reduction of labeled phenyl pentazole and warming. The appropriate mass spectrometric signals were detected, including those of the product azide anions upon MS/MS experiments. This provides strong evidence in support of our

ACS Paragon Plus Environment

The Journal of Physical Chemistry

claim for the first solution synthesis and detection of N_5^- in solution. Variations in the synthetic procedure support the conclusion that sodium metal is, by itself, too strong a reducer for this reaction and most probably produces the phenyl pentazole dianion, which decomposes to yield the azide anion directly. It appears as though the main bottleneck for this reaction is long reduction time needed when passivated sodium is used, a problem that might be ameliorated by employing a gentler reducing agent.

Dedication

This article is dedicated to the memory of the late Professor Yehuda Haas. Professor Haas was the main power behind this research, pushing it forward in health and sickness. We will always remember him fondly.

Acknowledgment

This research was not supported by any outside sources – only internal budgets were used.

Supporting Information. Exemplary full scale mass spectra.

References

- Bazanov, B.; Geiger, U.; Carmieli, R.; Grinstein, D.; Welner, S.; Haas, Y. Detection of Cyclo-N₅⁻ in THF Solution. *Angew. Chemie - Int. Ed.* **2016**, *55*, 13233–13235.
- Huisgen, R.; Ugi, I. Pentazole, I. Die Lösung eines Klassischen Problems der Organischen Stickstoffchemie. *Chem. Ber.* **1957**, *90*, 2914–2927.
- Ugi, I.; Huisgen, R. Pentazole, II. Die Zerfallsgeschwindigkeit der Aryl-Pentazole. *Chem. Ber.* 1958, *91*, 531–537.

- (4) Vij, A.; Pavlovich, J. G.; Wilson, W. W.; Vij, V.; Christe, K. O. Experimental Detection of the Pentaazacyclopentadienide (Pentazolate) Anion, Cyclo-N₅⁻. *Angew. Chemie* 2002, *114*, 3177–3180.
- (5) Östmark, H.; Wallin, S.; Brinck, T.; Carlqvist, P.; Claridge, R.; Hedlund, E.; Yudina, L.
 Detection of Pentazolate Anion (Cyclo-N₅⁻) from Laser Ionization and Decomposition of
 Solid P-Dimethylaminophenylpentazole. *Chem. Phys. Lett.* **2003**, *379*, 539–546.
- (6) Ugi, I. Pentazole. Angew. Chemie **1961**, 73, 172.
- Benin, V.; Kaszynski, P.; Radziszewski, J. G.; Radziszewski, G. Arylpentazoles Revisited:
 Experimental and Theoretical Studies of 4-Hydroxyphenylpentazole and 4 Oxophenylpentazole Anion. J. Org. Chem. 2002, 67, 1354–1358.
- Portius, P.; Davis, M.; Campbell, R.; Hartl, F. F.; Zeng, Q.; Meijer, A. J. H. M.; Towrie, M.
 Dinitrogen Release from Arylpentazole: A Picosecond Time-Resolved Infrared,
 Spectroelectrochemical, and DFT Computational Study. *J. Phys. Chem. A* 2013, *117*, 12759–12769.
- (9) Geiger, U.; Haas, Y. Photochemistry of Aryl Pentazoles: Para-Methoxyphenylpentazole. J.
 Phys. Chem. B 2015, 119, 7338–7348.
- (10) Geiger, U.; Haas, Y.; Grinstein, D. Photochemistry of an Aryl Pentazole in Liquid Solutions:
 The Anionic 4-Oxidophenylpentazole (OPP). *J. Photochem. Photobiol. A Chem.* 2014, 277, 53–61.
- (11) Bazanov, B.; Haas, Y. Solution Photochemistry of [P-(Dimethylamino)phenyl]pentazole

(DMAPP) at 193 and 300 nm. J. Phys. Chem. A 2015, 119, 2661–2671.

- Butler, R. N.; Hanniffy, J. M.; Stephens, J. C.; Burke, L. A. A Ceric Ammonium Nitrate N-Dearylation of N-P-Anisylazoles Applied to Pyrazole, Triazole, Tetrazole, and Pentazole Rings: Release of Parent Azoles. Generation of Unstable Pentazole, HN₅/N₅⁻, in Solution.
 J. Org. Chem. 2008, 73, 1354–1364.
- Butler, R. N.; Stephens, J. C.; Hanniffy, J. M.; Burke, L. a. First Generation of Pentazole (HN₅, Pentazolic Acid), the Final Azole, and a Zinc Pentazolate Salt in Solution: A New N-Dearylation of 1-(P-Methoxyphenyl) Pyrazoles, a 2-(P-Methoxyphenyl) Tetrazole and Application of the Methodology to 1-(P-Methoxyphenyl). *Tetrahedron Lett.* 2003, *45*, 1977–1979.
- (14) Schroer, T.; Haiges, R.; Schneider, S.; Christe, K. O. The Race for the First Generation of the Pentazolate Anion in Solution Is far from Over. *Chem. Comm.* **2005**, 1607–1609.
- (15) Perera, S. A.; Gregusova, A.; Bartlett, R. J. First Calculations of 15N- 15N J Values and New Calculations of Chemical Shifts for High Nitrogen Systems: A Comment on the Long Search for HN₅ and Its Pentazole Anion. J. Phys. Chem. A **2009**, 113, 3197–3201.
- (16) Zhang, C.; Sun, C.; Hu, B.; Yu, C.; Lu, M. Synthesis and Characterization of the Pentazolate Anion Cyclo- N_5^- in $(N_5)_6(H_3O)_3(NH_4)_4$ Cl. *Science*. **2017**, *355*, 374–376.
- (17) Zhang, C.; Yang, C.; Hu, B.; Yu, C.; Zheng, Z.; Sun, C. A Symmetric Co(N₅)₂(H₂O)₄·4 H₂O
 High-Nitrogen Compound Formed by Cobalt (II) Cation Trapping of a Cyclo-N₅⁻ Anion.
 Angew. Chem. 2017, 56, 4512–4514.

- (18) Geiger, U.; Haas, Y. Preparation of the Cyclopentazole Anion in the Bulk: A Computational Study. *J. Phys. Chem. B* **2016**, *120*, 6208–6214.
- Peled, E. The Electrochemical Behavior of Alkali and Alkaline Earth Metals in Nonaqueous
 Battery Systems- The Solid Electrolyte Interphase Model. *J Electrochem. Soc.* 1979, *126*, 2047–2051.



