Solvated Electrons in Organic Chemistry Laboratory

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SUPPLEMENT

The supplement is divided into three major sections:

SECTION 1: Instructor's notes, with the analysis and assignment of the ^{1}H NMR spectra of the substrate and reaction products, and an outline of the electronic structure calculation procedure.

SECTION 2: A detailed list of chemicals and associated hazards.

SECTION 3: Student instructions with a detailed description of the glassware, quantities of the reagents, procedures for conducting the experiment and analyzing the ^{13}C NMR spectra, and questions pertaining to this experiment.

SECTION 1 -- INSTRUCTOR NOTES:

(1.A) REDUCTION OF THE ALCOHOL TO AMINE:

The preparation of 2-phenylethaneamine (**2**) from the alcohol precursor, 2-amino-1-phenylethanol, APE, (**1**) is a moderately complex, intense and short laboratory project.

Figure S1: APE (A) and its dexydroxylation product (B)

The most time-consuming part of the experiment, production of liquid NH_3 by distillation of NH_4OH solution, typically takes between 30 min (the distillation setup ready, the Dewar flasks with 2-butanol have been stored in the refrigerator) to 1 hr. If starting from scratch – as we have been doing – additional time, needed to obtain dry ice from a local grocery store or gas station should be included; about one and a half to two pounds (depending on the starting conditions) of dry ice is sufficient for two batches of experiments. However, setting up the glassware for distillation of NH_4OH and trapping and handling liquid ammonia is an interesting and useful laboratory exercise that can be ported to other organic synthetic projects (e.g. preparation of sulfanilamide drugs). Although a single, dexterous, skillful and motivated person can relatively easily carry out all the procedures – including obtaining a ^{1}H and ^{13}C NMR spectrum – in one three-hour lab period, we advise that the project be assigned to a team of two to three students.

The ammonia production setup, however, could be shared by more than one lab team.

(1.B) THE REDUCTION REACTION:

The two versions of the reaction, (1) the reductive dehydroxylation of APE and (2) the partial reduction in the presence of an electron scavenger (inhibitor), are carried out the same way. A small amount (~ 0.14 g) of APE (or the inhibitor first and then APE) is quickly transferred to and dissolved in ~ 15 ml to 20 mL of liquid ammonia (hood!) to which 3 - 4 shots of elementary lithium are added. The reaction mixture - which instantly turns deep blue - should be vigorously stirred and the Li shots crushed with a glass rod. It takes several minutes for the liquid ammonia to evaporate and leave a beige-white paste (in the case of the uninhibited reaction). In case additional electron scavengers are added, the coloring of the reaction mixture is different as is the consistency and the color of the final semi-solid product. The inhibitors reported here - 1,2,4,5-benzene tetracarboxylic acid 1,2:4,5-dianhydride, (2,4-dinitrophenyl) hydrazine, N,N-dimethylaniline, 4-methoxy-1-benzamine – as well as other compounds we were testing as potential inhibitors (urea, 4-chlorophenol, hydroxylamine, 5-hydroxy-1H-indole) readily dissolve in liquid ammonia. We have tested the effectiveness of the inhibitors over the APE-to-inhibitor molar ratios from 1:1 (equimolar) to 50: 1 (2 molar % of the inhibitor)

NOTE 1.1: ABOUT THE CHEMICALS

All the chemical substances used in this experiment are standard, inexpensive chemicals, available from common commercial suppliers. (We purchased the substrate, 2-amino-1-phenyl ethanol (APE) from Sigma-Aldrich, stock # A-752405.) The Li- or Na-salts of 3,5-dinitrobenzoic acid are not commercially available and we prepared them by dissolving the solid 3,5-dinitrobenzoic acid – a poorly soluble material – in approx. 0.2 M aqueous solutions of base, with warming up to 40 – 45 °C and constant stirring. We tried LiOH, NaOH and $NaHCO_3$.and

eventually settled on sodium hydrogen carbonate as the reagent of choice. After the salt is formed the excess water could be removed either by lyophilization or slow evaporation. There is a warning that the dry dinitrobenzene salt could explode under mechanical stress but we have never had any, even potentially, hazardous situation during this preparation.

It is conceivable that ammonium 3,5-dinitriobenzoate will itself exhibit the same or comparable electron-capturing properties as its Na- and Li-salts so the inhibited reaction could be run by adding 3,5-dinitrobenzoic acid straight to the ammonia solution. It is well worth exploring this reaction variant as it would avoid the lengthy preparation of the alkali salts.

NOTE 1.2: THE NEXT STEP

Once liquid ammonia has evaporated and a solid product formed in the mortar (STUDENT NOTES, step 3.C.1) the paste could be rinsed off more efficiently and with a smaller amount (< 5 mL) of dilute HCl solution (0.5 to 3.0 M) rather than with distilled water. In this case one should only make sure that, before the extraction with $CDCl_3$, the pH of the aqueous phase is well into basic region or else the whole amine content will remain as a quaternary base, dissolved in the aqueous layer, and lost for subsequent analysis. The hallmark of the uninhibited reduction reaction is that Li + NH_3 is a dark-blue-purple solution, Fig. S2, while the addition of secondary electron scavengers results in reaction mixtures colored purple, honey-gold, or different shades of brown, like with 1,2,4,5-benzenetetracarboxylic acid 1,2:4:5-dianhydride, Fig. S3.

Figure S2: Li + NH_3(l)

Figure S3: Inhibitor + Li+NH_3(l)

CAVEAT # 1.1: In the early stages of the project, we would prepare both the uninhibited product and a series of partially inhibited products and store them as dry paste in a dessicator for subsequent analysis. However, an old product – a couple of days or weeks – would not dissolve in $CDCl_3$, nor in other deuterated solvents, $CDCN_3$ and d_6-DMSO, even at elevated temperature and with prolonged shaking. We ascribe this, highly annoying fact, to the tendency of the small, compact lithium cation to form low solubility salts *(Ref. S1)*. The lithium in the mixture binds to small amounts of water (probably condensed from the atmosphere by the cold liquid ammonia) and forms LiOH, which subsequently converts to Li_2CO_3, and then, likely, to practically insoluble Li_2O. We therefore suggest that the reaction be started and the reduction product transferred to the organic phase in <u>one laboratory session</u> or not delayed more than 24 hours.

<u>(1.C) NMR ANALYSIS:</u>

The ^{13}C NMR resonance signals, reported in the main article, are simple and easy to obtain using a spectrometer with a superconducting magnet and a relatively high signal-to-noise, S/N, ratio. We have used a BRUKER Avance 300 MHz spectrometer with a normal probe. In addition, we have recorded and analyzed the ^{1}H NMR spectra of the reaction substrate and product. The proton NMR spectrum of the substrate, APE, is rich and interesting and we have

subsequently used it to illustrate certain NMR features in a separate laboratory session. The proton NMR spectrum of 2-amino-1-phenylethanol is complex, due to diastereotopy - the phenomenon that protons on a Csp^3 center exhibit different chemical shifts due to partial stiffness of the alkane carbon skeleton and the diverse environment of the alkane protons. (This phenomenon is often encountered in organic chemistry lab, for example in cycloalkanes, making the NMR analysis of brominated cyclohexane - an excellent example of polar addition reactions products - rather difficult.) We have assigned the proton NMR resonances in APE using $^1H - ^1H$ double quantum correlation experiment, COSY, carried out using a BRUKER AMX 500 MHz spectrometer (the NMR Facility at Mayo Graduate School, Rochester, Minnesota.) First, we assign the very broad (FWHM ~ 9.1 Hz) peak at 2.04 ppm to the coalesced O-^{1}H, and N-^{1}H resonances. The H7 proton signal is centered at 4.63 ppm and the two H9 protons at 2.94 ppm and 2.79 ppm. Each proton signal is split into a doublet of doublets: the H9a and H9b are split by 12.81 Hz through geminal coupling $^2J_{Hab.}$ The 12.81 Hz doublet centered at 2.94 ppm is further split by 7.86 Hz through *cis/trans*-vicinal coupling with H7, $^3J_{H7H9a}$. The H9b doublet, centered at 2.79 ppm, is further split by 3.93 Hz into a doublet of doublets through *gauche*-vicinal coupling with H7. The H7 resonance is split into a 7.86 Hz by 3.93 Hz doublet of doublets through *cis/trans*-coupling with H9a (7.86 Hz) and *gauche*-vicinal coupling with H9b (3.93 Hz), Figure S4(a,b). (Notice that the labeling we use here and in the NMR spectra is meant to facilitate a comparison of the ^{1}H chemical shifts among the three different compounds – APE, the product amine, and the 1,4-cyclohexadiene intermediate – and is not a correct, systematic labeling of the corresponding compounds.) The phenyl protons are shifted slightly more downfield than expected; the nearest-neighbor H2 and H6 signals, anisotropic due to the through-space interaction with the amine protons, have resonances in the 7.34 ppm to 7.46 ppm

region. The H3, H5 resonances, asymmetrically split by coupling with H2 and H6, are in the 7.296 ppm to 7.311 ppm region, difficult to resolve due to the presence of a strong $CHCl_3$ solvent proton impurity at 7.278 ppm. This is to our knowledge the first assignment of the proton NMR resonances in 2-amino-1-phenyl ethanol.

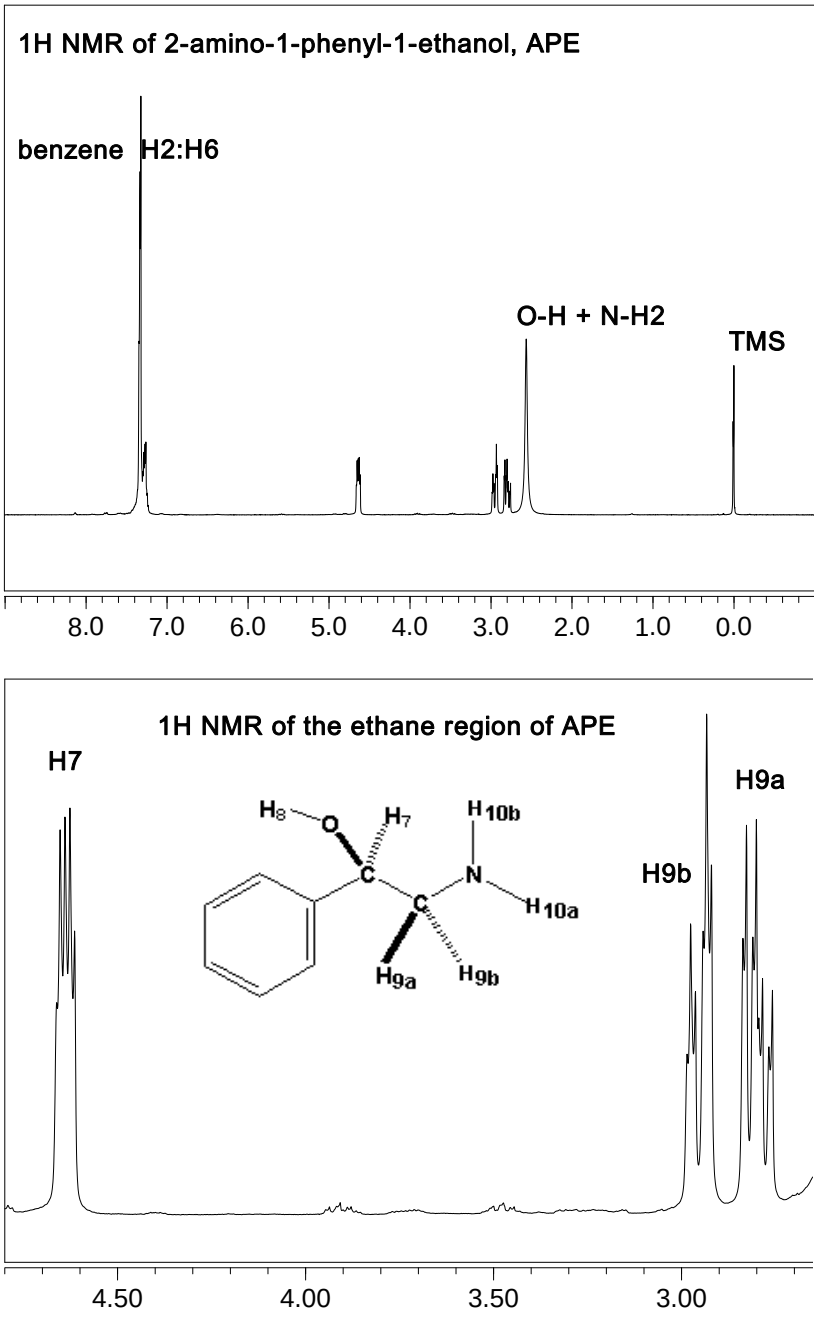


Figure S4(a,b): The assignment of the alkene ^{1}H resonances in the NMR spectrum of APE.

A comparison of the experimental NMR data and the NMR shifts calculated using first principles electronic structure methods point to the preferred conformation of APE, in accordance with our geometry optimization calculations and previously reported data *(Ref. S2)*. We find APE to be an interesting molecule, suitable for designing an advanced physical organic chemistry project based on NMR analysis and electronic structure calculations.

The product of APE reduction, 2-phenylethaneamine, shows a simple, isotropic proton NMR spectrum. The phenylethyl H7,H8 resonance is around 2.74 ppm and the ethylamine H9a,H9b resonance around 2.96 ppm. As expected, both peaks are split into triplet through the 6.8 Hz vicinal coupling, $^{3}J_{\mathrm{HiHj}}$. Particularly interesting are the ^{1}H spectra of the products of partially inhibited reduction of APE as they clearly show the alkene resonances, at 5.71 and 5.47 ppm, in accordance with the expected 1,4-cyclohexadiene product of the Birch reduction, Figure S5:

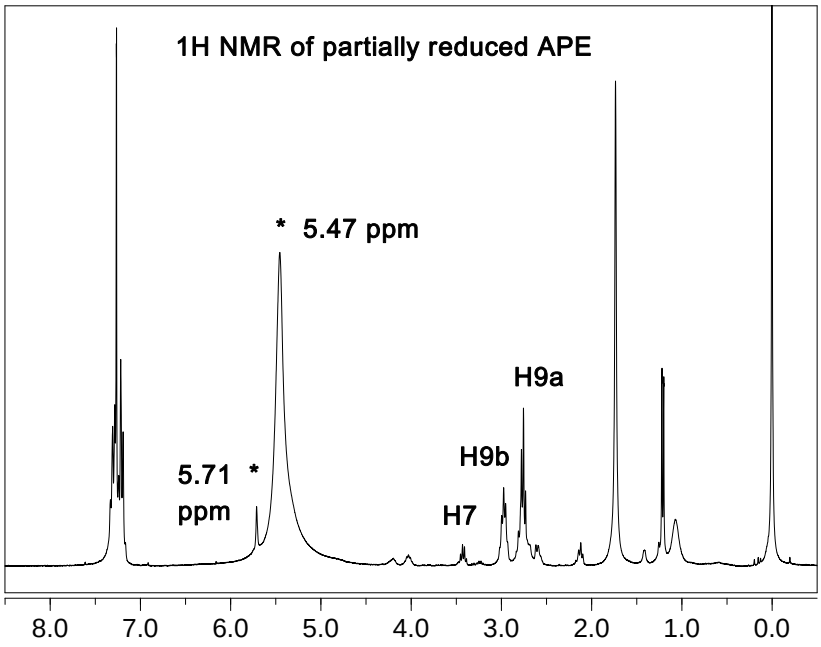


Figure S5: The ^{1}H NMR spectrum of a reaction mixture containing APE, the amine product, as well as cycloalkene intermediates (δ = 5.47 & 5.71 ppm) of the Birch reduction reaction.

(1.D) ELECTRONIC STRUCTURE CALCULATIONS:

We have used Gaussian 03W, the "Windows" version, installed on a 32-bit single-processor microcomputer, run under MicroSoft Windows XP operating system, for calculation of electron affinities. The graphical interface program, GaussView for Windows, was used to build molecular structures in graphical window, prepare and submit the computational job, and check the structural consistency of the energy-optimized molecule. As stated in the main article (Note 1), the electron affinity of each species is calculated as the difference between the total electronic energy of its radical anion and the total electronic energy of the same, neutral species, multiplied by minus one:

$$EA = - \{E(\text{radical anion}) - E(\text{neutral})\}$$

First, we calculate the total electronic energy of a neutral (so-called "closed-shell") molecule by the procedure of energy optimization ("opt"). For example, for neutral 3,5-dinitrobenzoic acid, at the approximation we have used (Perdew-Wang-91 functional at the 3-21G level of theory) we get for the total electronic energy:

$$E(N) = E(\text{UB+HF-PW91}) = -985.592361787 \text{ hartree}$$

Note that the energy is, following the long-entrenched practice in electronic structure calculations, given in hartrees per molecule (1 hartree = $4.3597482 * 10^{-18}$ J). In the next round, the same molecular structure is used in the input file only an electron is added, making a total of 119 electrons, *vs.* 118 electrons in the neutral species. This makes the molecule a radical anion so the total charge should be changed to -1 (from 0) and the total spin should be changed from 1

(singlet) to 2 (doublet). Using the same method of calculation we obtain for the total electronic energy of the radical anion:

$$E(RA) = E(UB+HF-PW91) = -985.642095023 \text{ hartree}$$

The negative DIFFERENCE between the two energies,

$$-\Delta E(RA,N) = -E(RA) + E(N) = +0.049733236 \text{ hartree},$$

is then multiplied by 2.625592, the conversion factor from hartree to kilojoule, to obtain:

$$\Delta E = 130.57 \approx 131 \text{ kJ/mol}.$$

This is the result we need - the electron affinity of one mole of 3,5-dinitrobenzoic acid. The EA of other species used as potential scavengers of solvated electron is calculated the same way. We suggest that the instructor carry out these calculations and prepares a list of potential scavengers. A better alternative is to create a computational project for junior or senior students enrolled in the physical chemistry course and have them design and carry out these calculations, and organize and present the results. This will give an opportunity to junior and senior students to collaborate and consult with younger colleagues in the sophomore organic chemistry course; it will also establish a clear purpose to their computational exercise.

ADDITIONAL BIBLIOGRAPHY:

[S1] Cotton, F.A., Wilkinson, G., "Advanced Inorganic Chemistry, 5th ed., Wiley-Interscience, **1988**, Ch. 4.1.

[S2] Graham, R. J., Kroemer, R. T., Monds, M., Robertson, E. G., Snock, L. C., Simons, J. P., "Infrared Ion Dip Spectroscopy of a Noradrenaline Analogue: Hydrogen Bonding in 2-Amino-1-phenylethanol and Its Hydrated Complex", *J. Phys. Chem. A,* **1999**, 103, 9706-9711.

SECTION 2 -- CHEMICALS – CAS INDICES & HAZARDS:

2-amino-1-phenylethanol, $C_6H_5CH(OH)CH_2NH_2$ CAS [7568-93-6]

No special precaution; avoid contact with skin

Ammonia, NH_3(l) CAS [7664-41-7]

Produced by distillation of NH_4OH solution; highly pungent vapors, hygroscopic, MUST be handled in a well ventilated fume hood.

Ammonium hydroxide, NH_4OH, 28-30 % solution in water CAS [1336-21-6]

Pungent vapors, should be handled in a fume hood.

1,2,4,5-Benzenetetracarboxylic acid 1,2:4,5-dianhydride, $C_{10}H_2O_6$ CAS [89-32-7]

No special precaution.

N,N-Dimethylaniline, $C_8H_{11}N$ CAS [121-69-7]

Avoid inhalation and contact with skin.

4-Methoxy-1-benzamine, C_7H_9NO CAS [104-04-9]

Avoid inhalation and contact with skin.

2-Phenylethylamine, $C_6H_5CH_2CH_2NH_2$ CAS [64-04-0]

No special precaution; neurologically active substance; avoid contact with skin.

2-Butanol CAS [78-92-2]

Inflammable liquid, avoid inhalation.

3,5-Dinitrobenzoic acid, 3,5-$(NO_2)_2$-C_6H_5COOH CAS [99-34-3] ,

Na-salt, FW 235.11, Li-salt, FW = 219.06; see Instructor's Notes.

Avoid contact with skin; dry compound subjected to mechanical stress can explode.

Calcium chloride, $CaCl_2$ (anhyd.) CAS [10043-52-4]

No special precaution.

Chloroform-*d*, deuterochloroform, $CDCl_3$ 99.8 % D CAS [865-49-6]

No special precaution; avoid inhalation.

(2,4-dinitrophenyl)hydrazine, $C_6H_6N_4O_4$ CAS [119-26-6]

Avoid contact with skin; dry compound subjected to mechanical stress can explode.

Hydrochloric acid, HCl, 1.5 – 3 M CAS [7647-01-0]

Highly corrosive acid, gloves and safety goggles must be worn.

Indol-5-ol (5-hydroxy-1H-indole), C_8H_7NO CAS [1953-54-4]

Possible neurophysiological effects, avoid contact with skin.

Lithium Li°, shots CAS [7439-93-2]

DANGER! Lithium MUST NOT come into contact with water; handle with extreme care! Store as a suspension in benzene.

Lithium hydroxide, LiOH CAS [1310-65-2]

Corrosive, harmful chemical; protective gloves & safety goggles should be worn.

Magnesium sulfate, $MgSO_4$(anhyd) CAS [7487-88-9]

No special precaution; it should be dried every 2- 4 weeks at 150 - 200 °C and subsequently stored in a dessicator.

1- or 2-propanol (techn.) CAS [71-23-8]

No special precaution; inflammable.

Sodium hydroxide, NaOH CAS [1310-73-2]

Highly caustic solid substance; protective gloves and goggles must be worn.

SECTION 3 -- STUDENT NOTES:

NOTE # 1: Read the ARTICLE and all auxiliary material required by instructor.

NOTE # 2: Read the CHEMICALS section; pay special attention to most hazardous chemicals.

NOTE # 3: Prepare the pre-lab document from this material.

NOTE # 4: When the experiment is finished dispose properly of ALL chemicals.

NOTE # 5: Prepare a lab report according to course guidelines and submit it.

(3.A) SELECTING AND WEIGHING THE CHEMICALS:

(3.A.1) Weigh 0.001 mol of 2-amino-1-phenylethanol,APE

(3.A.2) Weigh 0.06 to 0.003 mol of elementary lithium, shots,

CAUTION: Keep the Li shots on filter paper, away from the lab sink and water !

(3.A.3) Weigh 0.001 to 0.00002 mol of any of the inhibitors from the list.

NOTE: The first part of the experiment, ammonia production (B), and APE reduction (C), must be carried out in a fume hood.

(3.B) AMMONIA PRODUCTION:

(3.B.1) PREPARATION OF 2-BUTANOL/DRY ICE SLURRY:

Obtain one to one-and-a-half pound (lb) of dry ice (solid CO_2). Wear protective mittens (or two pairs of Latex or similar type laboratory gloves) and, using tools – a small hammer is most suitable – crush the dry ice into 2 – 3 cm chunks. Pour 150 - 200 mL 2-butanol (technical grade) into a 750 mL – 1 L Dewar and start adding dry ice chunks. You should start adding small pieces as there is a large temperature difference between the solid CO_2 (< -40 °C) and the

liquid alcohol (room temperature) and butanol will intensely foam and overflow the Dewar flask due to the released gaseous CO_2. After the liquid cools down you may add larger pieces of solid CO_2; occasionally stir the mixture with a rod. The goal here is to a create a slurry at temperature bellow -34 °C (b.p. NH_3 -33.35 °C); this operation will take 30 – 40 minutes.

(3.B.2) AMMONIA PRODUCTION AND COLLECTION:

The glassware:

(1) 600 mL to 1 L Erlenmeyer flask if a heating plate is used (or an equal size round bottom flask if a heating mantle is used),

(2) 500 mL Erlenmeyer flask (or a 500 mL suction flask), and

(3) 100 mL or 50 mL round bottom flask.

The assembly:

Assemble the glassware as in Scheme 3 in the article or as in the picture below, Figure S6. Stopper the large flask with a two-hole rubber stopper equipped with a longer tube with a release valve and a shorter glass tube with ¼" hose (e.g. a Tygon® tube). Connect the hose to the 500 mL flask, immerse the flask in a batch cooled to between - 4 ºC and - 6 ºC (salted-ice-water can be used but a Dewar flask with 2-butanol and smaller amounts of dry ice work better) and let it cool down for at least 10 – 15 min. Connect the other outlet at the 500 mL flask (the H_2O vapor trap) to a 100 mL or 50 mL round bottom flask, RBF. Connect the other outlet of the small RBF to a drying tube filled with dry $CaCl_2$ or other hygroscopic material. Immerse the small RBF into a 2-butanol/dry ice slurry cooled down to -50 ºC or lower.

The procedure:

Fill the large, 600 mL – 1000 mL, flask up to ~ 40% of volume with NH_4OH, 28-30 % aqueous solution, stopper it, place it in a heating mantle and start heating. (Prior to heating you may want to add a Claisen connector and a 250 mL separatory funnel, Figure S6, which will allow you almost continuous replenishing of NH_4OH.) After the ammonium hydroxide starts boiling the water will start condensing in the 500 mL flask immersed in the ice bath and the pungent smell of NH_3 is detected even in a well-ventilated hood. Connect the second trap (the 100 mL flask) and immerse it the in 2-butanol / dry ice slurry. (NOTE: If the second trap stays immersed in the low-temperature slurry long before the NH_4OH solution starts boiling it will – as the coldest spot in the laboratory – condense the H_2O vapors. The small amount of liquid water will dilute the freshly condensed ammonia and thwart the reaction.)

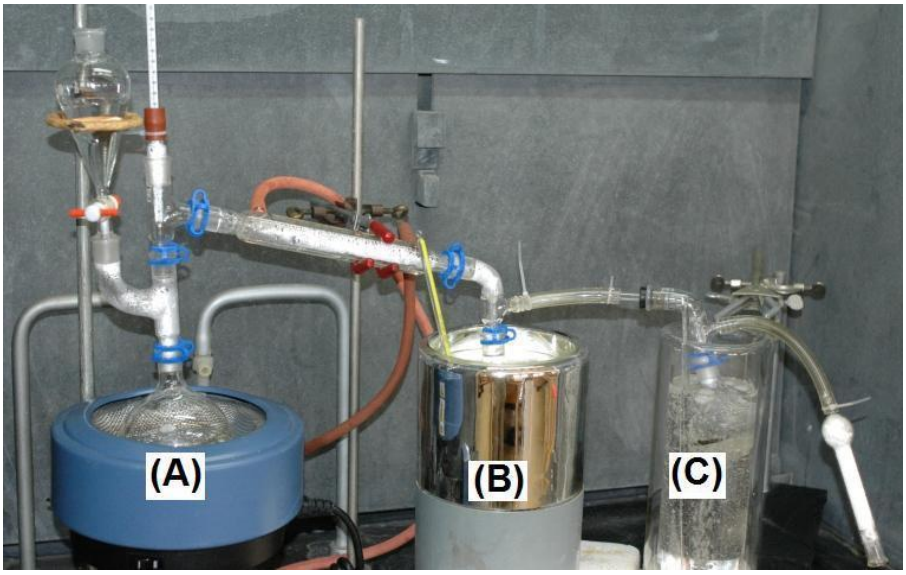


Figure S6: The NH_4OH boiler (A), the $H_2O(l)$ condenser (B), and the $NH_3(l)$ condenser (C).

(3.C) THE REDUCTION REACTION:

(3.C.1) REDUCTION OF APE WITHOUT INHIBITOR:

The reaction:

After about 20 mL of liquid ammonia has been collected, separate the large flask with NH_4OH from the heater and transfer the liquid ammonia to a dry, thermally insulated mortar (packing material chips will do). Add, in rapid succession and with constant and vigorous stirring, 0.001 mol of APE and then 5- to 6-fold molar amount of Li shots (typically ~ 0.04 g). Strong deep-purple-blue coloration of the solution will develop upon the addition of elementary lithium (Figure S2). Break the Li shots with a glass rod as best and as fast as you can. As ammonia evaporates within several minutes the reaction mixture turns into a white paste and the reaction is finished. Transfer the paste using a rubber policeman and, using a plastic squirt bottle, rinse it off with a small amount of distilled water or a small amount of diluted (0.5 to 3 M) HCl solution into a 125 mL (or smaller) separatory funnel.

Product extraction:

Check the pH of the aqueous solution in the separatory funnel and adjust it to no lower than 8. Extract the organic phase from the solution with 3 - 5 mL of $CDCl_3$; transfer the organic phase (the bottom layer!) to a dry test tube and repeat the extraction with another 1 - 2 mL of $CDCl_3$. Collect the two organic extracts in the same test tube and add anhydrous $MgSO_4$ to remove excess water; you will need to filter the $MgSO_4/CDCl_3$ suspension through a small fine glass-wool plug and repeat the drying procedure. Take a 0.6 to 0.7 mL aliquot of the dry $CDCl_3$ solution, transfer it to an NMR tube and stopper the tube. You are now ready for NMR spectroscopy.

(3.C.2) REDUCTION OF APE IN THE PRESENCE OF AN INHIBITOR:

Inhibited reaction & product extraction:

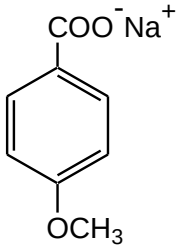
Everything is done in the same way as in (C.1) except that both the pre-weighed APE and the inhibitor are added to and dissolved in liquid NH_3 before the addition of Li shots. The color of the reaction mixture and the final product will vary from clear violet (5-hydroxy-1H-indole) to honey-gold (1,2,4,5-benzenetetracarboxylic acid 1,2:4,5-dianhydride). Wash the product paste off to a separatory funnel (adjust pH to ≈ 8) and extract the aqueous solution/suspension, first with 3 - 5 mL of $CDCl_3$ and then again with 1 - 2 mL of $CDCl_3$; pool the $CDCl_3$ extracts together and dry it with anhydrous $MgSO_4$ until no lumps form.

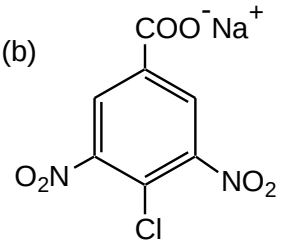
(3.D) NMR ANALYSIS:

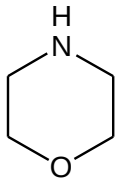
Pipet 0.6 – 0.7 mL of the dry $CDCl_3$ solution into an NMR tube, cap it, put a spinner on the tube and adjust its height. Insert the NMR tube into a well-tuned and shimmed spectrometer, run a ^{13}C decoupled experiment and record a ^{13}C spectrum; 16 - 32 scans should be sufficient when using a NMR spectrometer equipped with a superconducting magnet. Refer to Figure 1(a) in the article. The ^{13}C spectrum of the reaction mixture is easy to interpret: the 74.2 ppm line (close to the large C-D triplet of the $CDCl_3$ solvent, at 78 ppm) indicates the presence of the alcoholic group carbon, ^{13}C-O. This line is observed in the ^{13}C NMR spectrum of the starting material, APE, and the ^{13}C NMR spectrum of an inhibited reduction product. The other ethane carbon resonance of APE, ^{13}C-NH_2, is observed at 49.2 ppm. If the experiment is run without an inhibitor the substrate is dehydroxylated to 2-phenylethylamine. As expected, the ^{13}C-O resonance at 74.2 ppm will be gone and replaced by the phenylethyl carbon resonance at 40.1 ppm, Fig. 1(b) in the article.

(3.E) QUESTIONS, PROBLEMS:

(1) The goal of inhibition is to introduce into the reaction mixture a compound that will capture an NH_3-solvated electron comparably well or even more effectively than the substrate, 2-amino-1-phenylethanol, APE (a derivative of benzyl alcohol). How would you rank the following compounds (best = first) as potential inhibitors of the Li/NH_3-reductive dehydroxylation of APE? [Hint: You may think that an inhibitor acts both as a species which is "chemically similar" to the substrate (e.g. a derivative of benzene) and also strongly electrophilic.]

(a) 

(b) 

(c) 

ANSWER (1):

(2) After shaking the water solution of the reaction products with $CDCl_3$ you place the separatory funnel into a clamped ring and let the organic and aqueous layers separate. By checking the pH of the upper, aqueous layer, you find its pH to be around 5. Are you sure you have transferred most of the product, a primary arylalkyl amine, to the $CDCl_3$ layer? Explain

your answer. [Hint: Check the pKa of primary amines and determine in what form they are likely to exist around pH 5.]

ANSWER (2):

(3) When ^{13}C NMR spectroscopy is used to monitor the reaction, the absence of the ^{13}C-O resonance in the product mixture indicates that reductive dehydroxylation of APE has been carried out successfully. However, addition of 5-hydroxy-1H-indole or 4-methoxy-1-benzamine into the reaction mixtures as possible electron scavengers also introduces an alcohol or ether group and could mask the progress of the dehydroxylation of APE. Is this true? [Hint: Check the ^{13}C NMR resonances [ppm] of Csp^3- and Csp^2- oxygen derivatives.]

ANSWER (3):