SAFE HYDROGENATION OF ORGANIC COMPOUNDS AND THEIR PROPERTY STUDIES

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ABSTRACT

In this work, chemical reduction of various compounds having double, triple bond or aromatic to single bond using a safe continuous flow hydrogenation instrument-H-cube and their physical and chemical property changes are studied. Due to flammability of hydrogen gas, forms an explosion mixture with air and difficulties in work-up has replaced with safe hydrogenation with H-cube having hydrogen generator from electrolysis of water. Here we stabilized the conditions like pressure and temperature for various compounds such as dyes, N-aromatics, chalcone and aliphaticyne compounds. The results obtained from the experiments of this study, in learning the hydrogenation of multiple bonds, will be able to be used as training aids for study of toxic, dye, active drug etc. analysis by physical, chemical and biological changes.

Keywords: Hydrogenation; Aromaticity; H-cube; Ivy

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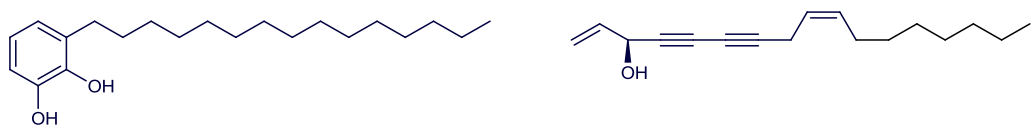
1. INTRODUCTION

Ivy, famously known as evergreen garden plant (figure 1a) in the genus *Hedera*, family Araliaceae natives of Eurasia and north Africa but later have been introduced to many countries and chosen as air-filtering plant by National Aeronautics and Space Administration (NASA) in association with the Associated Landscape Contractors of America (ALCA).[1] These plant species have ability to eliminate significant amounts of human carcinogens like benzene, formaldehyde and trichloroethylene from the air and along with this it will help to decreasing effects of sick building syndrome. Due to these advantages (compatible climates, evergreen foliage, traditional ground cover for planting under trees and air-purification) its cultivation increased enormously. However, the sap of truncated Ivy plant or all parts of some species more toxic that can cause symptoms that include skin irritation, burning throat, fever and rash when in contact, even if only reaches to cause allergic symptoms. Poison ivy contains an irritating, oily sap toxins called 'Urushiol' and 'Falcarinol'. Where 'Urushiol',[2] are naturally existing organic compounds that have the catechol skeleton structure and diphenol functionality but with 3-*n*-alk-(en)-yl have zero, one, two and three double bonds in the C_{15} side chain and 'Falcarinol',[3] a poly-yne with two carbon-carbon triple bonds and double bonds and with one chiral hydroxyl functionality (figure 1b).

(a)

(b)



3-Pentadecyl-1,2-benzenediol
(Urushiol I)

(3S,9Z)-Heptadeca-1,9-diene-4,6-diyn-3-ol
(Falcarinol)

Figure 1(a): Ivy, foliage plant, (b): Chemical structures of 'Urushiol I' and 'Falcarinol'

Thus, it was forecast that how to minimize the toxicity of 'Urushiol I' and 'Falcarinol' in Ivy. Our tentative hypothesis was that the toxicity of Ivy due to its chemical ambivalence structure and would be reduced if the chemical bonds of toxic substances were transformed. If keenly observing the structure of poisonous substances it showed a way to alter the

structure by reduce multiple bond to single bond is one of method instead of functionalizing hydroxyl group may minimize toxicity. Considering that sigma bonds in these structures are not participate in any reactions, so we focused on finding a way to reduce multiple bonds of poisonous substances into single bonds. We eventually concluded that the hydrogenation might be a key to solving this problem. Hydrogenation is a chemical reaction of molecular hydrogen and in presence of catalyst such as nickel, palladium or platinum to reduce or saturate organic compound. Functional group reductions (e.g., alkene, alkyne, nitro) and deprotections (e.g., benzyl) are very common in catalytic hydrogenations.[4]

2. EXPERIMENTS

2.1.Apparatus

Hydrogenation reactions are carried out on Parr 3916 shaker hydrogenation apparatus (figure 2a) purchased from Parr instrument company, Illinois, USA and ThalesNano H-cube hydrogenation reactor (figure 2b) from Budapest, Hungary.

Figure 2 (a): Parr Hydrogenation Apparatus (b):H-Cube

2.2.Reagents

3-Decyn-1-ol, (2*E*)-1,3-diphenyl-2-propen-1-one (chalcone), 1*H*-Indole-2,3-dione (isatin), 3-hydroxypyridine (3-pyridinol), 2,6-dichloropyridine, 2-(ethyl{4-[(***E***)-(4-nitrophenyl)diazenyl]phenyl}amino)ethanol (Disperse Red 1), were purchased form Aldrich (USA) and used without further purification and (2*E*)-1-[2,4-bis(benzyloxy)-6-hydroxyphenyl]-3-[3,4-bis(benzyloxy)phenyl]-2-propen-1-one was synthesized in laboratory by known procedure.[5] All other reagents and solvents were purchased from TCI Chem. Ltd. (Japan). Solvents were dried and purified prior to used, according to standard procedures.

2.3.Methods

1) Hydrogenation with Parr apparatus

The reactant (10 mg) was dissolved in a soluble solvent (10 mL) in Parr glass bottle (100 mL) followed by careful addition of suitable catalyst (0.1 M) and then arranged in Parr hydrogenation apparatus, adjusted pressure (1 bar to maximum 6 bar) and temperature up to 80 ^{o}C, continued until TLC shows complete consumption of starting material. After that passed through celite to filter the catalyst, concentrate the solvent and purified by silica gel column chromatography to get pure reduced product.

2) Hydrogenation with H-Cube

The solvents were chosen based on the solubility and chemical properties of each reactant. Then, the reactants (10 mg) were dissolved in a given solvent (100 mL) (0.1 mg/mL concentration) injected into the equipment. After the injection, the hydrogenation reactions of the chosen substances were conducted several times under the variable pressures and temperatures in order to examine the minimum temperature and pressure conditions needed for activating the hydrogenation reaction. After that collected the product from outlet, progress of the reaction was monitored by TLC chromatography, if still starting material remained kept the reaction again by subtle change in pressure and temperature. After TLC showed complete conversion of starting material, concentrated under vacuum rotor to remove solvent and purified by column chromatography to get pure desired product.

2.4.Characterization

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer (BRUKER, Germany), IR spectra were recorded on a FT-IR-6300 (JASCO, Japan) spectrometer and Gas chromatography-mass spectrometric (GC-MS) analyses were carried out with Hewlett-Packard 6890 & 5973 system (AGILENT, USA).

3. RESULTS AND DISCUSSION

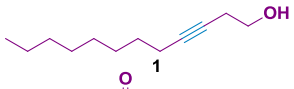
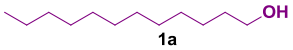
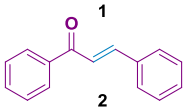
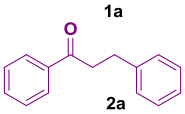
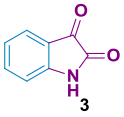
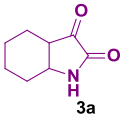
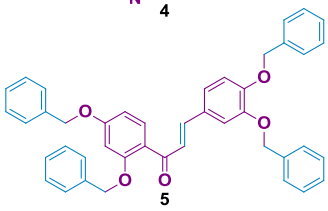
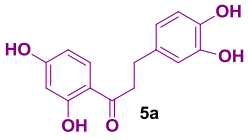
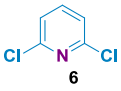
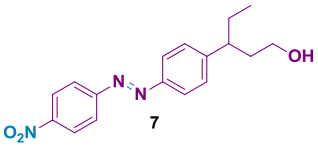
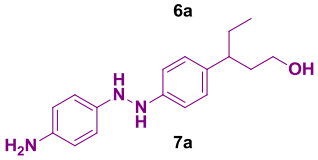
Generally in laboratory or industrial reduce organic compounds using Parr hydrogenation apparatus or simple hydrogen balloon for hydrogenation, So we used Parr instrument to reduce few organic compounds with aromaticity while kept high temperature and pressure even maintain longer times it is un-capable of reduce aromatic double bonds

along with this some disadvantages like chance of explosion, hazard, difficult catalyst addition, work-up and, volatile and flammable solvent usage. To overcome these problems replaced Parr with H-cube,[6-8] a continuous flow reactor where flow of substances is combined with hydrogen, generated in-situ from the electrolysis of water and easy to maintain pressure up to 100 bar and temperature to 100 ^{o}C respectively, within 5 minutes product emerges for fast reduction and optimization. To understand the chemical reduction organic transformation for undergraduate school elected H-cube as effective instrument. Once the dissolved reactant is injected into the reactor, it goes through continuous hydrogenation reactions in a system and turns into the hydrogenated product with just a few touches. Aside from its easy manipulation, the reactor provides every aspects of operation through the touch-screen panel and is considered safe with no external storage of hydrogen necessary. The reactor, also, allows precise manipulation of temperature and pressure, ensuring more credible experimental results. Easy catalyst change (catcarts) is one of the other benefits of this reactor. Therefore, in this study we have used H-cube to study efficient reduction of readily available unsaturated compounds and subtle differences in combination of catalyst, pressure and temperature led to products in high yield.

Along with multiple bond structures, several distinctive properties (e.g. color) were taken into account when selecting reactants since those properties would noticeably change after going through the hydrogenation process. In consideration of those conditions, seven compounds were selected for the study: 3-decyn-1-ol (**1**), (2*E*)-1,3-diphenyl-2-propen-1-one (chalcone) (**2**), 1*H*-Indole-2,3-dione (isatin) (**3**), 3-hydroxypyridine (3-pyridinol) (**4**), (2*E*)-1-[2,4-bis(benzyloxy)-6-hydroxyphenyl]-3-[3,4-bis(benzyloxy)phenyl]-2-propen-1-one (**5**), 2,6-dichloropyridine (**6**), and 2-(ethyl{4-[(*E*)-(4-nitrophenyl)diazenyl]phenyl}amino)ethanol (Disperse Red 1) (**7**) as illustrated in table 1.

Here, we have carried out hydrogenation of compound **1** in presence of Pd catcart under 20 bar H_2 pressure and at 20 ^{o}C using H-cube yielded dodecanol **1a**. Completion of reaction is predicted from TLC chromatography by solvent elute (ethyl acetate:hexane, 3:7), where starting material was slowly charred in potassium permanganate ($KMnO_4$) solution, blue color spot with anisaldehyde solution and product didn't show any spot in $KMnO_4$, light green color with anisaldehyde. In this case product **1a** was confirmed by thin layer chromatography technique.

Table 1.Hydrogenation of organic compounds using H-cube

Entry	Starting material	Color	Catcarts	Product	Color	Pressure (bar) / Temparature (°C)	Yeild (%)
1.	 1	Colorless	Pd	 1a	Colorless	20 / 20	94%
2.	 2	Colorless	Pd	 2a	Colorless	10 / 20	93%
3.	 3	Browinsh yellow	Pt	 3a	Colorless	30 / 30	90%
4.	 4	Light yellow	Pt	 4a	Colorless	50 / 70	91%
5.	 5	Yellow	Pt	 5a	Colorless	30 / 30	93%
6.	 6	White	Pt	 6a	Colorless	40 / 70	93%
7.	 7	Red	Pd	 7a	Black	10 / 20	89%

The solution of (2*E*)-1,3-diphenyl-2-propen-1-one (**2**) dissolved in ethyl acetate was injected in the H-Cube (10 bars, 20 ^{o}C), Pd was used for the catalyst to get 3-phenylpropiophenone (**2b**) in 93% yield, which was confirmed by IR absorption bands at 1609 cm^{-1} (C=C strech) for *trans*-olefin **2**, while this band disappeared in **2b** (figure 4).

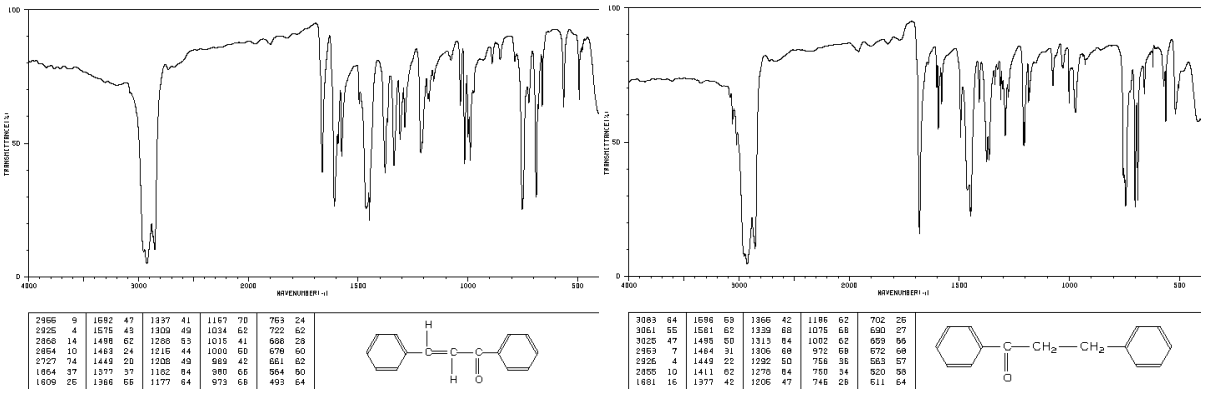


Figure: 4 IR spectrum of compound 2 and 2a

The solution of isatin **3** in methanol was injected in to the H-cube, adjusted pressure to 30 bars at 30 ^{o}C and Pt was used for the catalyst to achieve compound **3a** in 90% yield. Progression of the reaction was checked through TLC (Anisaldehyde, 30% EtOAc-Hexane). Since high pressure and temperature are required for hydrogenate aromaticity of isatin, Pt catcart was used instead of Pd catalyst. In the reaction, reduction of double bonds in benzene rings can be observed by noticeable color changes from brownish yellow (staring material) to transparent (product).

The solution of 3-hydroxypyridine **4** in methanol was reduced by the H-Cube (50 bar, 70 ^{o}C) using Pt catalyst afforded 3-piperidinol in 91% yield, which was confirmed by disappearing of aromatic carbon at δ 125, 126, 137,139 and 156 in ^{13}C NMR spectrum (figure 5) and GC-MS spectrum showed *m/z* value change from 95 to 101 also confirmed same (figure 6).

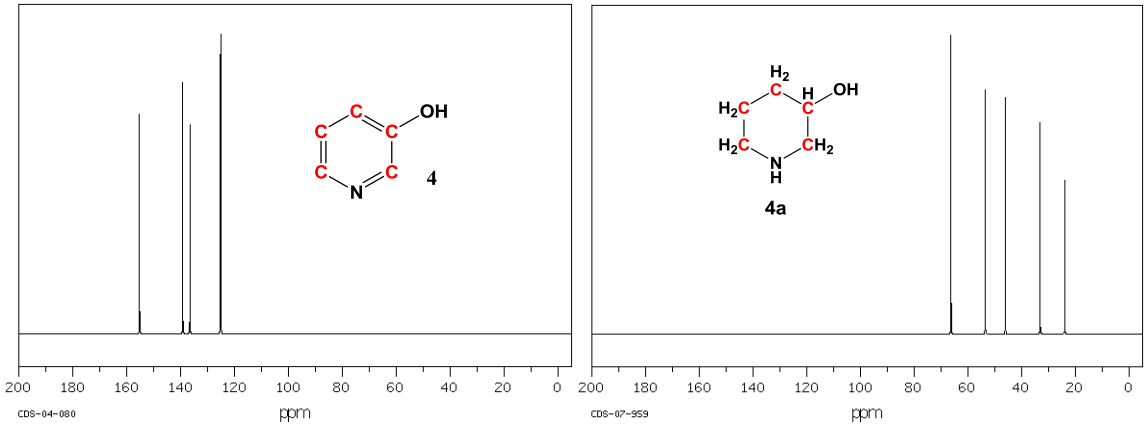


Figure 5: ^{13}C NMR spectrum of compound 4 and 4a

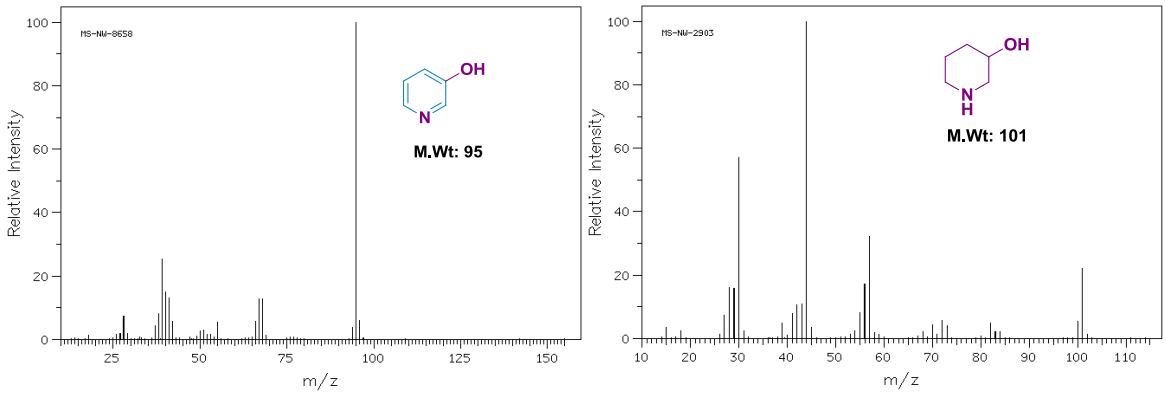


Figure 6: GC-MS spectrum of compound 4 and 4a

The solution of compound **5** in ethyl acetate was injected in to the H-Cube, stabilized pressure 30 bar, temperature 30 ^{o}C) used Pt catalyst to get tetra-ol product **5a** in 30% yield.

Here, progress of reaction observed by color change from starting yellow to transparent product and further confirmed with thin layer chromatography technique by anisaldehyde charring and UV chamber. In this reaction, four benzyl groups were deprotected along with double bond reduction.

We injected the solution of 2,6-dichloropyridine (**6**) in methanol in the H-Cube (40 bars, 70 ^{o}C) in presence of Pd catcart to gave piperidine product **6a** in 93% yield. Reaction was monitored by TLC and reduction was confirmed through the NMR spectra analysis which clearly shows disappearance of aromatic protons δ 7.4 and 7.6 (figure 7).

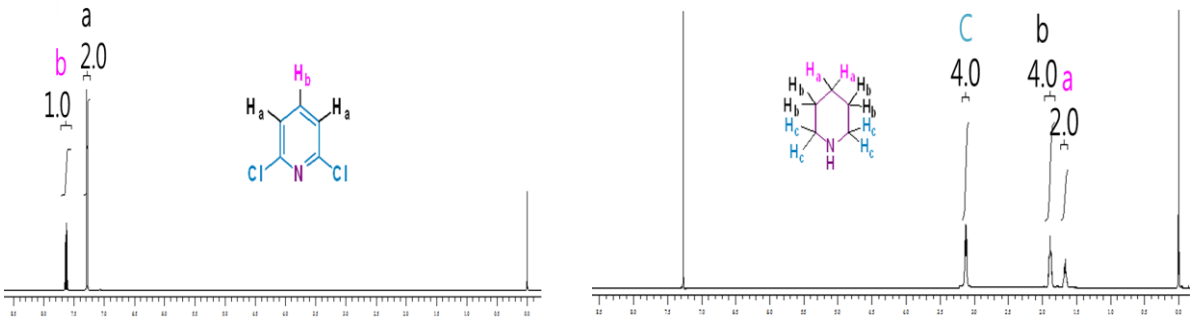


Figure 7: ^{1}H NMR spectrum of compound 6 and 6a

The solution of Disperse Red 1 (**7**) in methanol subjected to hydrogenation in presence of Pd catcart under 10 bar H_2 pressure and at 20 ^{o}C using H-Cube to afford product **7a** in 89% yield. Progress of reaction monitored by color change from red to light yellow product and then slowly to black due to unstable hydrazine functionality in product derived from azo group (N=N). Further reduction was confirmed with thin layer chromatography technique by using ninhydrin charring and UV chamber.

All these products confirmed by either by ^{1}H, ^{13}C NMR, IR, mass spectrometric analyses or TLC and are in accordance with that of reported ones. All products prepared using H-cube and experimental results on the hydrogenation of sampled multiple compounds is convenient enough to reduce other dyes, natural products and drugs.

4. CONCLUSIONS

In summary, we conducted hydrogenation of different compounds which have multiple bonds through the H-Cube with subtle varying different pressure and temperature conditions of the reaction and one could change the properties of compounds through hydrogenation. Depending on the kind of multiple bonds of the compounds, difference of the

color between the reactant and product was clear. Suitable catalysts, pressure, and temperature of the reaction made the reduction of double bonds from benzene and pyridine rings possible. In this way, multiple bonds in poisonous compounds can be reduced, so the toxicity of the compound can change. As well, one can conduct studies about property change through hydrogenation of medicines like aspirin, dyes like indigo and unsaturated fatty acid.

5. REFERENCES

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	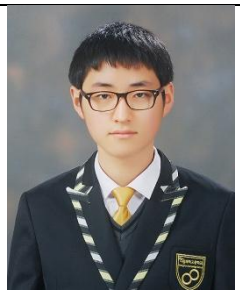	
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