A Greener Oxidation Reaction

A case study prepared by Beyond Benign as part of the Green Chemistry in Higher Education program: A workshop for EPA Region 2 Colleges and Universities

A Greener Oxidation Reaction

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Summary:
Oxidation reactions are commonly performed in the organic chemistry laboratory course. The reactions are typically performed using chromium compounds, such as pyridinium chlorochromate (PCC) and sodium dichromate dihydrate, two of the most common oxidizing reagents. Chromium compounds are known to be carcinogenic and many also have reproductive and developmental hazards associated with them. A greener method for performing this experiment would be very valuable.

Reduction in waste and purchasing costs:

For every semester this reaction is implemented with 100 students, there is an estimated ***cost savings of $204.46*** in purchasing and waste disposal costs and a ***decrease in 0.67 gallons liquid and 0.56 pounds solid waste.*** The greener version of the Alcohol Dehydration also results in the ***elimination in the use of 375 g sodium dichromate dehydrate, 395 mL cyclohexanol and 750 mL diethyl ether***, all of which have human health

Background:
This case study is a result of an EPA Region 2 Source Reduction grant[1] titled *Green Chemistry in Higher Education: A Workshop for Region 2 Colleges and Universities*. The Green Chemistry in Higher Education workshop was carried out at Siena College on July 18-21, 2013. 29 faculty members participated from 20 different institutions in New York and New Jersey. The workshop consisted of three main focus areas: green chemistry case studies for lecture and course work, green chemistry laboratory exercises, and toxicology and environmental impact.

During the workshop participants were able to test a variety of greener laboratory exercises for introductory and organic chemistry courses. One of the labs was a greener oxidation reaction that avoids the use of traditional oxidizing reagents, such as chromium compounds. The greener method uses a molybdenum compound to perform the reaction. Two faculty members indicated they are implementing the greener oxidation reaction at their institutions: Abby O'Connor at the College of New Jersey (200 students each semester) and Andrea Stadler at St. Joseph's College (40-50 students each semester).

[1] **Disclaimer: Although the information in this document has been funded wholly or in part by the United States Environmental Protection Agency under assistance agreement X9-96296312 to Beyond Benign, it has not gone through the Agency's publications review process and, therefore, may not necessarily reflect the views of the Agency and no official endorsement should be inferred.**

Additional Resources for Green Chemistry in General Chemistry and Beyond:

Greener Educational Materials (GEMs) Database (University of Oregon)

- Website: http://greenchem.uoregon.edu/gems.html
- Description: Searchable database with Green Chemistry educational materials uploaded by faculty members and educators world-wide
- Most curriculum is available for download (free-of-charge) or with primary literature information
- Google map of Green Chemistry educators

American Chemical Society's Green Chemistry Institute

- Website: www.acs.org/greenchemistry
- Description: Green Chemistry Resources for educators and students
- Experiments and Curriculum available for download
- List of ACS books on Green Chemistry

Green Chemistry Commitment

- Website: www.greenchemistrycommitment.org
- Description: A program of Beyond Benign to adopt Green Chemistry Learning Objectives in higher education.
- Case studies are available, university highlights, and curriculum resources

Beyond Benign

- Website: www.beyondbenign.org
- Description: Green Chemistry Curriculum available on-line (free-of-charge)
- Regional Outreach and Community Educational Events

GCEdNet - Green Chemistry Education Network

- Website: http://cmetim.ning.com/
- Description: A place where Green Chemistry educators share resources
- Blogs, discussions and chat rooms

University of Scranton Greening Across The Chemistry Curriculum

- Website: http://www.scranton.edu/faculty/cannm/green-chemistry/english/drefusmodules.shtml
- Description: Green Chemistry modules available for download
- Power point presentations, hand-outs available

Carnegie Mellon University Institute for Green Science

- Website: http://igs.chem.cmu.edu/
- Description: Green Chemistry modules available for download
- Power point presentations, hand-outs available

Traditional Experiment:

Most organic chemistry laboratory procedures for the oxidation of alcohols to aldehydes or ketones involve the use of hazardous oxidizing agents, such as chromium compounds. Some of the most ubiquitous of these compounds is pyridinium chlorochromate (PCC) and sodium dichromate dihydrate, which are known carcinogens that also have reproductive and developmental hazards associated with them.

Chemicals used and hazards:

The chemicals that are typically used in this experiment are listed below, along with a list of the hazards. The amounts are estimated based on common procedures.[2]

Oxidation Reactions
Traditional Experiment

Chemicals avoided per class of 100 students:
375 g sodium dichromate dihydrate
395 mL cyclohexanol
750 mL diethyl ether

Table 1. Chemicals used and health and safety information for traditional experiment:

Chemical:	**Amount per group of 2 students:**	**Flammability:**[3]	**Human health toxicity:**[4]	**Aquatic toxicity:**[4]
sodium dichromate dihydrate	7.5 g	n/a	Chronic toxicity: Carcinogen (IARC Group 1), reproductive and developmental hazards LD50 (oral, rat) 50 mg/kg	High toxicity
acetic acid, 1 M	20 mL	n/a	*Causes skin and eye burns and damage*	Low toxicity
cyclohexanol (0.948 g/mL)	7.5 g (7.9 mL)	Combustible Liquid NFPA Code: 2 Flash Point: 67°C	Moderate Toxicity LD50 (oral, rat) 1,400 mg/kg; LD50 (rabbit, dermal) 1,000 mg/kg	Moderate Toxicity LC50 (fish, 96 hr) 705 mg/l; EC50 (daphnia, 48 hr) 500 mg/l; EC50 (algae, 72 hr) 29.2 mg/l
water	50 mL	n/a	n/a	n/a
sodium chloride	8 g	n/a	Low toxicity	Low toxicity
Anhydrous Diethyl ether	15 mL	*Highly Flammable NFPA Code: 4 Flash Point: -45C*	*Low toxicity* LD50 (oral, rat) 1,215 mg/kg; LD50 (dermal, rabbit) 14.2 g/kg	*Low toxicity* LC50 (fish, 96 hr) 2,560 mg/l; EC50 (daphnia, 24 hr) 165 mg/l
3M sodium hydroxide	10 mL (1.2 g/10 mL)	n/a	*Causes severe skin burns and eye damage*	*Moderate Toxicity* LC50 (fish, 96 hr) 45.4-125 mg/l; EC50 (daphnia, 48 hr) 40.4 mg/l
sodium chlorde solution, aqueous, saturated	15 mL (5.4 g/15 mL)	n/a	Low toxicity	Low toxicity

[2] Williamson, K. L., Maters, K. M., Macroscale and Microscale Organic Experiments, Sixth Edition, 2011, Cengage Learning, Inc.
[3] NFPA codes can be found here: http://en.wikipedia.org/wiki/NFPA_704#Red
[4] Human health and aquatic toxicity data was gathered from Globally Harmonized Safety Data Sheets, which can be obtained from Sigma-Aldrich [http://www.sigmaaldrich.com/united-states.html].

Traditional Experiment, Continued:

The purchasing and waste disposal costs associated with this procedure are estimated in the following table. Purchasing costs were estimated based on prices available from Sigma-Aldrich:[5]

Total amounts of chemicals used and disposed of per class of 100 students:

- ***375 g (0.83 lb) sodium dichromate dihydrate***
- ***395 mL (0.1 gal) cyclohexanol***
- ***750 mL (0.2 gal) diethyl ether***
- ***1.55 gallons liquid waste, 1.11 lb solid waste***

Oxidation Reactions

Traditional Experiment

Volume of waste and purchasing and waste disposal costs per class of 100 students:

1.55 gallons liquid and 1.11 lb solid waste

$326.04 in purchasing and disposal costs

Table 2. Purchasing and waste disposal costs:

Chemical:	Amount per 100 students:	Waste disposal cost[6]	Purchasing cost:[5]	Purchasing cost per 100 students:	Waste disposal cost per 100 students:	Total cost (per 100 students)
sodium dichromate dihydrate	375 g (0.83 lb)	$1.35/lb	$155.00, 1 kg	$58.13	$1.12	$59.25
acetic acid, 1 M	1 L (0.26 gal)	$11.27/gal	$36.50, 1 L	$36.50	$2.93	$39.43
cyclohexanol (0.948 g/mL)	395 mL (0.1 gal)	$11.27/gal	$43.10, 1 L	$17.02	$1.13	$18.15
water	2.5 L (0.66 gal)	$11.27/gal	n/a	$0.00	$7.44	$7.44
sodium chloride	400 g (0.88 lb)	$1.35/lb	$39.90, 500 g	$31.92	$1.19	$33.11
Anhydrous Diethyl ether	750 mL (0.2 gal)	$11.27/gal	1 L - $129.00	$96.75	$2.25	$99.00
3M sodium hydroxide	500 mL (0.13 gal) (60 g/500 mL)	$11.27/gal	$54.30, 500 g	$6.52	$1.47	$7.98
sodium chlorde solution, aqueous, saturated	750 mL (0.2 gal, 270 g/750 mL)	$11.27/gal	$39.90, 500 g	$21.55	$2.25	$23.80
calcium chloride	125 g (0.28 lb)	$1.35/lb	$150.00, 500 g	$37.50	$0.38	$37.88
TOTAL	**1.55 gallons and 1.11 lb**			**$305.89**	**$20.16**	**$326.04**

Total purchasing and waste disposal costs per class of 100 students:

- ***$305.89 in purchasing costs***
- ***$20.16 in waste disposal costs***
- ***$326.04 total cost***

[5] Sigma-Aldrich [http://www.sigmaaldrich.com/united-states.html, Accessed July 18, 2014].
[6] Waste disposal costs are based on the EPA Cost Calculator Tool [http://www.epa.gov/p2/pubs/resources/measurement.html#calc, accessed December 2014].

Greener Oxidation Reaction

A Greener Approach

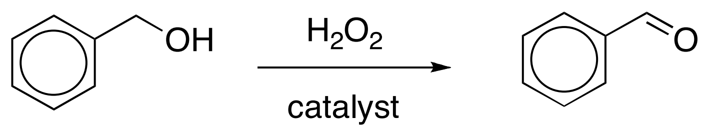
Volume of waste and purchasing and waste disposal costs per class of 100 students:

0.88 gallons of liquid and 0.55 lb solid waste

$121.60 in purchasing and disposal costs

A Greener Approach:

Professor Irv Levy at Gordon College developed a greener approach to the traditional oxidation reaction that eliminates the use of chromium compounds. The new approach uses a molybdenum catalyst as a replacement for the traditional reagents. In this reaction, the oxidizing agent is formed from sodium molybdate to make an efficient catalyst that is activated by aqueous hydrogen peroxide:



Chemicals used and hazards:

The chemicals that are used in the greener experiment are listed below, along with a list of the hazards. The amounts are estimated based on Professor Levy's procedure in Appendix A.

Table 3. Chemicals used and health and safety information for greener approach:

Chemical:	Amount per group of 2 students:	Flammability:[3]	Human health toxicity:[4]	Aquatic toxicity:[4]
sodium molybdate dihydrate	0.3 g	n/a	*Low toxicity*	*Low toxicity*
4 M HCl	0.5 mL + 1 mL water	n/a	*Causes severe burns and eye damage*	
benzyl triethyl ammonium chloride	0.525 g in 3 mL water	n/a	*Causes skin, eye and respiratory irritation*	*Low toxicity*, LC50 (fish, 96 hr) 161 mg/l
water	5 mL	n/a	*Low toxicity*	*Low toxicity*
benzyl alcohol	5 mL	Low Flammability, NFPA Code: 1, Flash Point: 101°C	*Moderate Toxicity* LD50 (oral, rat) 1,230 mg/kg; LD50 (dermal, rabbit) 2,000 mg/kg	*High toxicity*, LC50(fish, 96 hr) 10 mg/l; EC50 (daphnia, 24 hr) 55 mg/l
hydrogen peroxide, 3%	60 mL	n/a	*Low toxicity* *LD50 (oral, mouse) 2000 mg/kg; LD50 (dermal, rat) 4060 mg/kg; LC50 (inh, rat) 2000 mg/m*	*Low toxicity*
sodium sulfate	5 g	n/a	*Low toxicity* LD50 (oral, mouse) - 5,989 mg/kg	*Moderate aquatic toxicity* LC50 (fish, 96 hr) - 120 mg/l; LC50 (fish, 96 hr) - 4,380 mg/l

[3] NFPA codes can be found here: http://en.wikipedia.org/wiki/NFPA_704#Red

[4] Human health and aquatic toxicity data was gathered from Globally Harmonized Safety Data Sheets, which can

Greener Oxidation Reaction
A Greener Approach

Volume of waste and purchasing and waste disposal costs per class of 100 students:
0.88 gallons of liquid and 0.55 lb solid waste
$121.60 in purchasing and disposal costs

A Greener Approach, Continued:

The purchasing and waste disposal costs associated with this procedure are estimated in the following table. Purchasing costs were estimated based on prices available from Sigma-Aldrich:[5]

Total amounts of chemicals used and disposed of per class of 100 students:
- ***15 g sodium molybdate dehydrate***
- ***25 mL 4M HCl***
- ***26.3 g benzyl triethyl ammonium chloride in 150 mL water***
- ***0.88 gallons liquid waste, 0.55 lb solid waste***

Table 4. Purchasing and waste disposal costs:

Chemical:	**Amount per 100 students:**	**Waste disposal cost**[6]	**Purchasing cost:**[5]	**Purchasing cost per 100 students:**	**Waste disposal cost per 100 students:**	**Total cost (per 100 students)**
sodium molybdate dihydrate	15 g (~15 mL of liquid waste) (0.0003 gal)	$11.27/gal	$79.50, 100 g	$11.93	$0.05	$11.97
4 M HCl	25 mL 4M HCl (8.2 mL conc. HCl)(75 mL liquid waste, 0.02 gal)	$11.27/gal	500 mL - $60.10 (conc. Solution)	$0.99	$0.23	$1.21
benzyl triethyl ammonium chloride	26.25 g in 150 mL water (~175 mL liquid waste, 0.05 gal)	$11.27/gal	$32.40, 100 g	$8.51	$0.56	$9.07
water	25 mL (0.0066 gal)	$11.27/gal		$0.00	$0.07	$0.07
benzyl alcohol	250 mL (0.066 gal)	$11.27/gal	$211.50, 1 L	$52.88	$0.74	$53.62
hydrogen peroxide, 3%	3 L (0.8 gal)	$11.27/gal	$1.77, 16 oz bottle (0.125 gal)	$11.33	$9.02	$20.34
sodium sulfate	250 g (0.55 lb)	$1.35/lb	500 g - $49.10	$24.55	$0.74	$25.29
	0.88 gal and 0.55 lb			**$110.19**	**$11.41**	**$121.60**

Total purchasing and waste disposal costs per class of 100 students:
- ***$110.19 in purchasing costs***
- ***$11.41 in waste disposal costs***
- ***$121.60 total cost***

Greener Alcohol Dehydration
Summary

Waste avoided:
Reduction in 0.67 gallons liquid and 0.56 lb solid waste
Avoids use of chromium compounds
Cost comparison:
Reduction in purchasing and disposal costs of $204.44

Traditional Experiment Summary:

Total amounts of chemicals used and disposed of per class of 100 students:

- ***375 g (0.83 lb) sodium dichromate dihydrate***
- ***395 mL (0.1 gal) cyclohexanol***
- ***750 mL (0.2 gal) diethyl ether***
- ***1.55 gallons liquid waste, 1.11 lb solid waste***

Total purchasing and waste disposal costs per class of 100 students:

- ***$305.89 in purchasing costs***
- ***$20.16 in waste disposal costs***
- ***$326.04 total cost***

A Greener Approach Summary:

Total amounts of chemicals used and disposed of per class of 100 students:

- ***15 g sodium molybdate dehydrate***
- ***25 mL 4M HCl***
- ***26.3 g benzyl triethyl ammonium chloride in 150 mL water***
- ***0.88 gallons liquid waste, 0.55 lb solid waste***

Total purchasing and waste disposal costs per class of 100 students:

- ***$110.19 in purchasing costs***
- ***$11.41 in waste disposal costs***
- ***$121.60 total cost***

Conclusions:

In summary, there is a drastic cost savings (a reduction of $204.46) for the greener oxidation reaction. The greener procedure still uses some chemicals with some known hazards, such as benzyl alcohol, which has moderate human toxicity and high aquatic toxicity. However, there still remains a significant benefit to humans and the environment in the greener procedure due to the avoidance of chromium compounds.

APPENDIX A: Selective Oxidation of Benzyl Alcohol to Benzaldehyde

Keti Assor[*], Irvin Levy[*‡], Erin Thames[‡] and Rowan Walker[‡]
Salem State University[*] and Gordon College[‡]

Background

Traditionally oxidation of alcohols to aldehydes requires the use of hazardous, heavy-metal reagents, such as pyridinium chlorochromate (PCC). In fact, PCC has been widely considered an appropriate agent for the oxidation, appearing in many undergraduate textbooks as the only viable method to produce aldehydes from alcohols. Both PCC and the usual solvent for its reaction, dichloromethane, are hazardous, cancer suspect agents. In this particular reaction, an environmentally safer oxidizing agent is formed from sodium molybdate to make an efficient catalyst that is activated by aqueous 3% hydrogen peroxide. In addition, hydrogen peroxide serves not only as an activating agent, but also as the solvent for this transformation.

Purpose

This experiment provides an excellent example of selective oxidation. In addition it demonstrates the synthesis and use of a catalyst in reaction. Other green lessons include replacement of a hazardous reactant with a safer alternative, the elimination of hazardous solvents, and reduction of waste.

Procedure

Preparation of tetrakis(benzyltriethylammonium) octamolybdate catalyst

Scheme I:

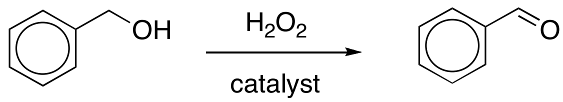
$$\begin{array}{l} 8\ Na_2MoO_4\ + \\ 12\ HCl\ + \\ 4\ BnEt_3N^{(+)}\ Cl^{(-)} \end{array} \longrightarrow [BnEt_3N]_4Mo_8O_{26} + 16\ NaCl + 6\ H_2O$$

Method:
To prepare the catalyst, sodium molybdate dihydrate (0.30 g; 1.2 mmol), and 4 M HCl (0.5 mL; 2.0 mmol) were added to a vial. About 1 mL of water was added to complete dissolution. Into a second vial benzyl triethyl ammonium chloride (BTEAC) (0.525 g; 2.30 mmol) and about 3 mL water were stirred until dissolved. The BTEAC solution was heated at 70 °C with stirring. To the stirred solution was added the molybdate solution dropwise. After addition was complete, the solution was stirred for an additional five minutes, then removed from heat and vacuum filtered.

The solid was washed with about 5 mL water while on the filter. The catalyst produced could be used wet or saved for later use.

Preparation of Benzaldehyde

Scheme II:



Method:

For preparation of benzyaldehyde, benzyl alcohol (5 mL; 50 mmol) was added to a 100 mL round bottom flask containing catalyst (dry weight 0.25 g; 0.2 mol%). Next, 60 mL of 3%(w/w) hydrogen peroxide was added to the flask. The mixture was then refluxed gently for one hour then cooled to near room temperature. The product was isolated by codistillation (simple distillation setup) into centrifuge tubes, yielding benzaldehyde and water in the distillate. Tubes were spun on centrifuge to hasten separation of the layers. Product was removed with a pipet, dried over sodium sulfate, then filtered. The mass and IR spectrum of the product were recorded.

Prelab

1. In this oxidation reaction, hydrogen peroxide is reduced to water. What is the balanced reaction for the oxidation step?
2. How many millimoles of hydrogen peroxide are in a 3%(w/w) solution of peroxide? Recall that (w/w) means mass of solute per mass of solution. To answer this you will need the density of the solution, estimating that a 3% solution has density is 1.0 g/ml.
3. Look up information, hazards, and safety on all materials used in this procedure.
4. What makes the benzaldehyde oxidation reaction *selective*?
5. What is the atom economy of each reaction scheme?
6. What is the approximate e-factor of each part of this synthesis?

References

1 Guo, Ming-Lin; Li, Hui-Zhen Li. Selective oxidation of benzyl alcohol to benzaldehyde with hydrogen peroxide over tetraalkylpyridinium octamolybdate catalysts. *Green Chem.* **2007,** 9, 421-423.

2 ACS. Selection from "Introduction to green chemistry". **2002**. Web access: http://domin.dom.edu/faculty/jbfriesen/chem254lab/atom_economy.pdf

3 Anastas, Paul T.; Warner, John C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, 1998.

4 Levy, Irvin J. The goal is zero; E-factor as a green chemistry metric. Web access: http://www.cs.gordon.edu/~ijl/visualizingWaste/

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