UMASS Boston
CENTER FOR GREEN CHEMISTRY

PBI Pressure BioSciences Inc.

Environmentally Benign Reduction of Organic Compounds in Water under High Hydrostatic Pressure

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Green Chemistry works toward sustainability by

- Making chemical products that **do not harm** either our health or the environment,
- Using industrial processes that **reduce or eliminate** hazardous chemicals, and
- Designing more efficient processes that **minimize** the production of waste materials.

*P. J. Dunn, A. S. Wells, M. T. Williams, Green Chemistry in the Pharmaceutical Industry, **2010**., Wiley-VCH*

Our aims

- Develop an **environmentally benign** process:

  Reduction of ketones using 50-50% Ni–Al alloy in water under high hydrostatic pressure (**40 000 psi**)

- **Extend** the process for a broad scope of ketones

Reduction of ketones

To **ALCOHOLS**

- Catalytic hydrogenation **(Pt, Rh, Ru, Ni…)**
- Hydrides and complex hydrides **(NaBH4, LiALH4…)**
- Microorganisms **(Beauveria sulfurescens)**

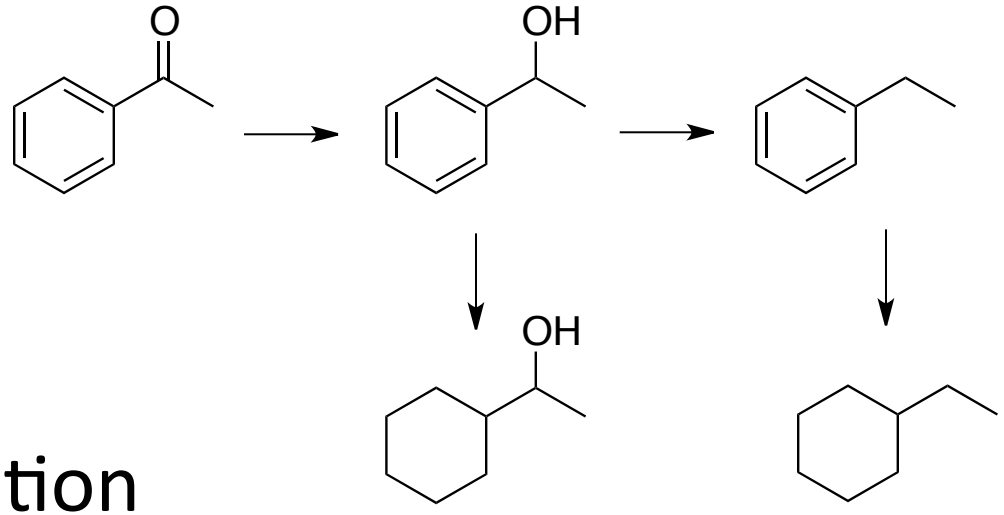
Name reactions: Grignard reaction, Meerwein-Ponndorf-Verley reaction

To **HYDROCARBONS**

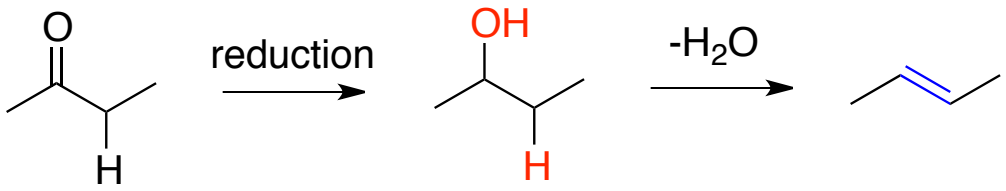
- Wolff-Kishner reduction **(NH2NH2, NaOH, Δ)**
- Clemmensen reduction **(HCl, Zn)**

Reduction of ketones to *alcohols OR alkanes OR alkenes*?

- Hydrogenation or overhydrogenation followed by hydrogenolysis

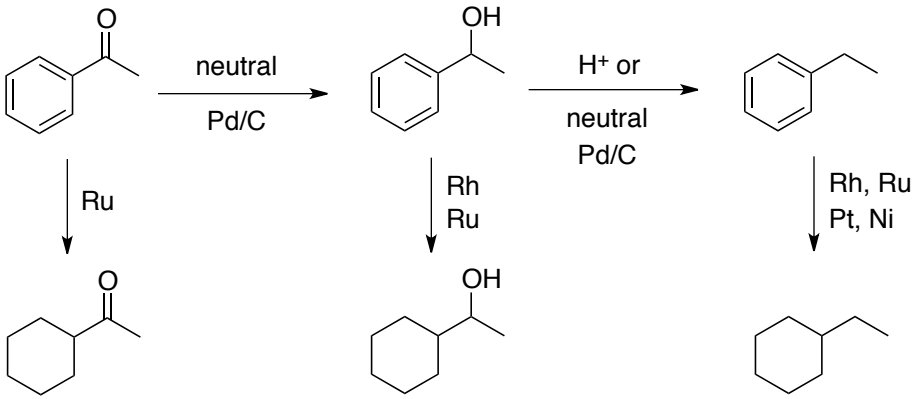


- Dehydration

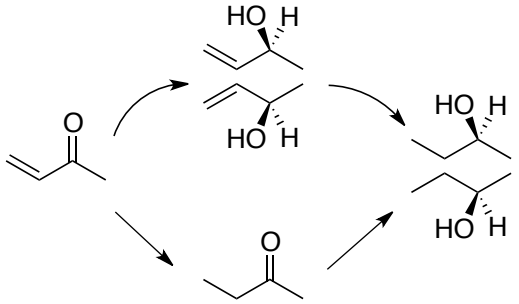


Competing reactions

- Keto group *vs* phenyl group



- Keto group *vs* C=C double bond



Raney-Nickel alloy

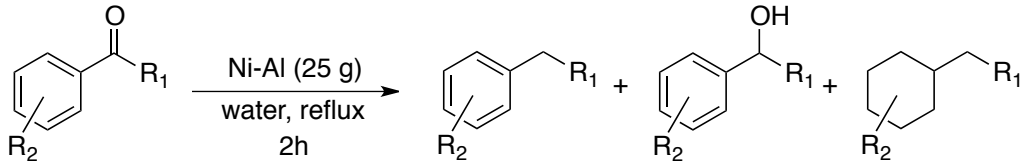
- Commercial Na-Ni alloy: 50 % Ni - 50 % Al ($NiAl_3$, Ni_2Al_3)

- Preparation:
  $2\ Al + 2\ NaOH + 6\ H_2O \rightarrow 2\ Na[Al(OH)_4] + 3\ H_2$

  removes Al -> generates H_2 => Ni activation

Raney-Nickel alloy as an effective reducing agent

1.



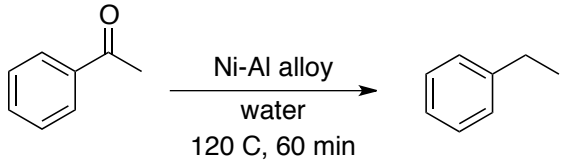
R_1=Me, R_2=H

Conversion [%]	Alloy	Yield [%]		
97.5	Ni-Al	97.1	0.4	-
18.9	Co-Al	0.9	18.0	-
20.1	Cu-Al	(+)	20.1	-
26.2	Fe-Al	(+)	26.2	-

R_1	R_2
$-CH_3$	-H
$-CH_2CH_3$	-H
$-CH_2CH_2CH_3$	-H
$-CH(CH_3)_2$	-H
$-CH_3$	4-CH_3-
$-CH_3$	3-CH_3-
$-CH_3$	2-CH_3-
$-C_6H_5$	-H

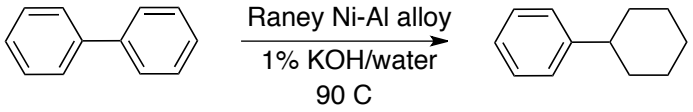
*K. Ishimoto, Y. Mitoma, S. Nagashima, H. Tashiro, G. K. S. Prakash, G. A. Olah, M. Tashiro, Chem. Commun. , **2003**, 514–515*

2.



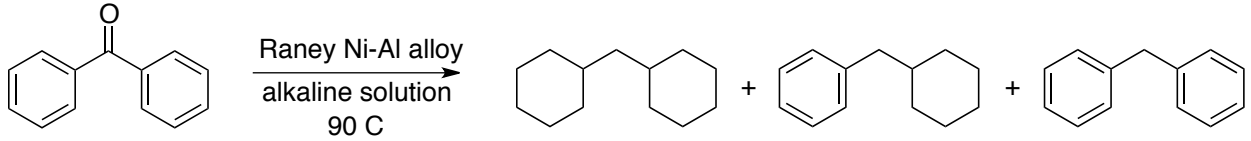
*A. Miyazawa, M. Tashiro, G. K. S. Prakash, G. A. Olah, Bull. Chem. Soc. Jpn. **2006**, 79, 791–792*

3.



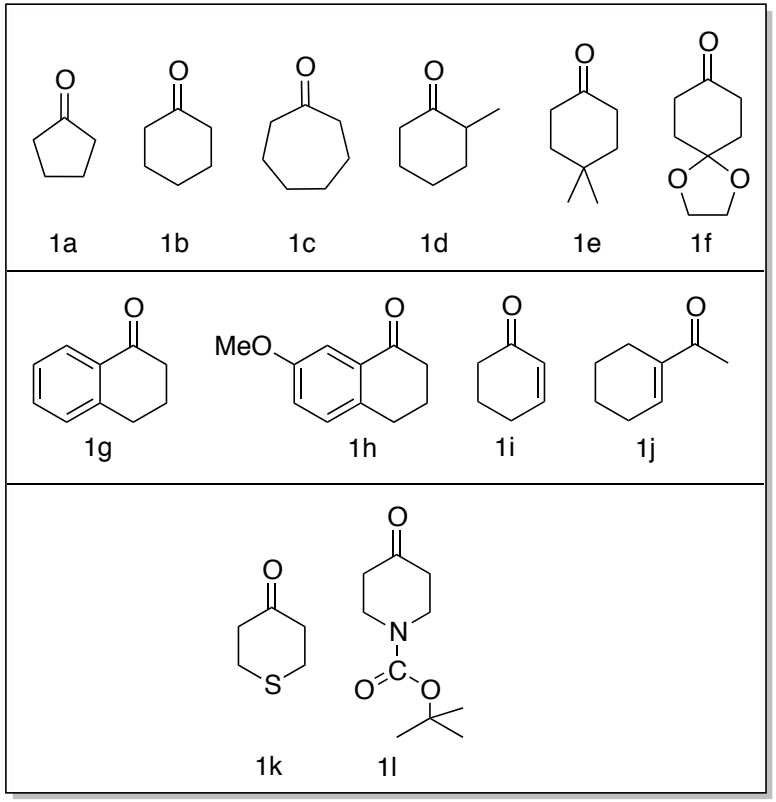
*T. Tsukinoki, T. Kanda, G-B. Liu, H. Tsuzuki, M. Tashiro, Tetrahedron Lett., **2000**, 41, 5865-5868*

4.



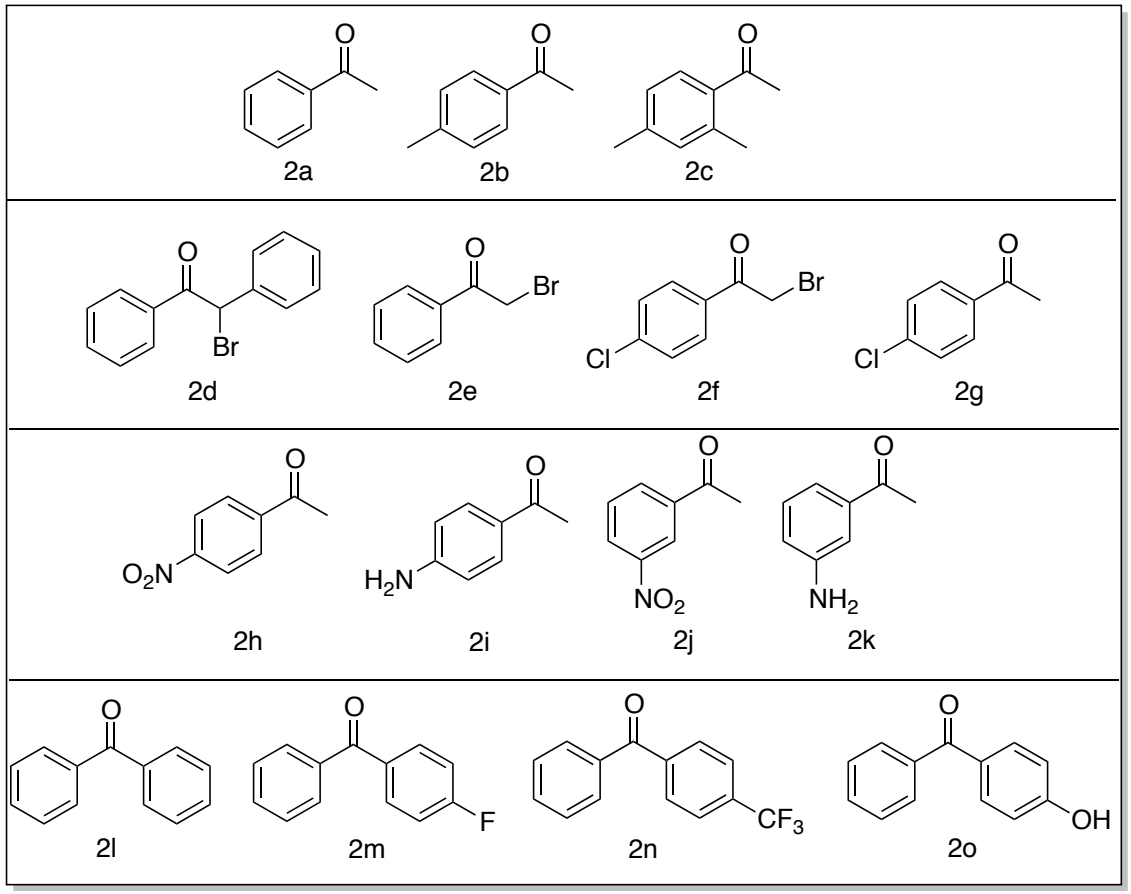
*G-B. Liu, H-Y. Zhao, J-D. Zhu, H-J. He, H-J. Yang, T. Thiemann, H. Tashiro, M. Tashiro, Synt. Commun., **2008**, 38, 1651–1661*

Cyclic ketones



- Cycloalkanones
- Allylic ketones
- Heteocyclic ketones

Acetophenones/Benzophenones



- Acetophenone derivatives
- Halogenated ketones
- Acetophenones with EWG
- Benzophenones

Environmentally benign process under 40 000 psi

Barocycler HUB440

Maximum pressure: 58 kpsi
Pressure accuracy: +/- 2 kpsi
Temperature range: 4 to 80 °C
Chamber construction: stainless steel

Manual and analog signal external control
Compact and portable
Rapid pressure change (full pressure in less then 2 sec)

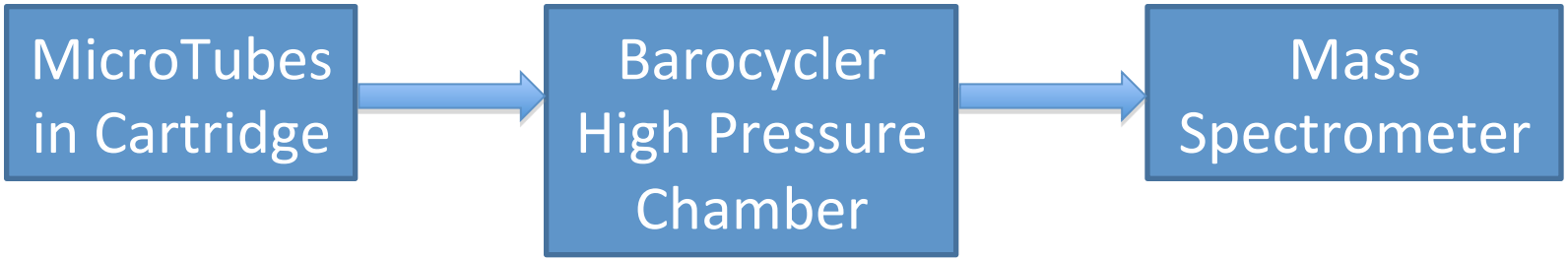
MicroTubes

FEP tube, PTFE cap
Highly inert
Chemical resistant

Workstation

Space saving:
48 samples

Pressure enhanced processes



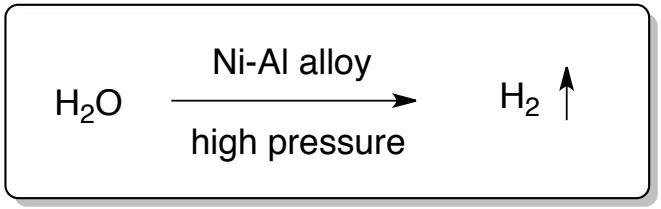
Reaction conditions:

0.03 mmol substrate
0.25 mmol 50-50 % Ni-Al alloy
110 µL water

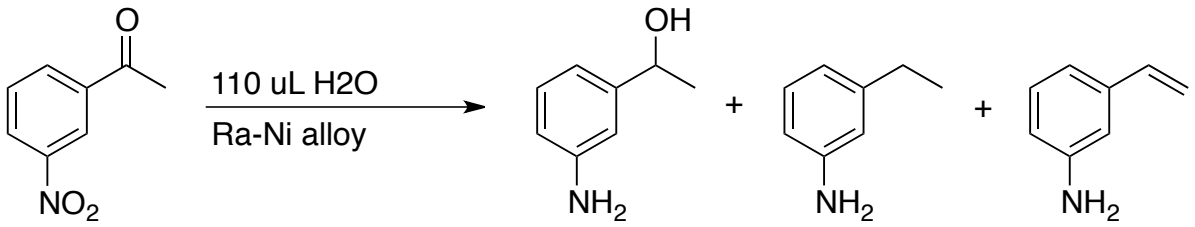
40 000 psi
1-16 hours

in situ hydrogen generation

Agilent 6850 **gas chromatograph-**5973 **mass spectrometer system**

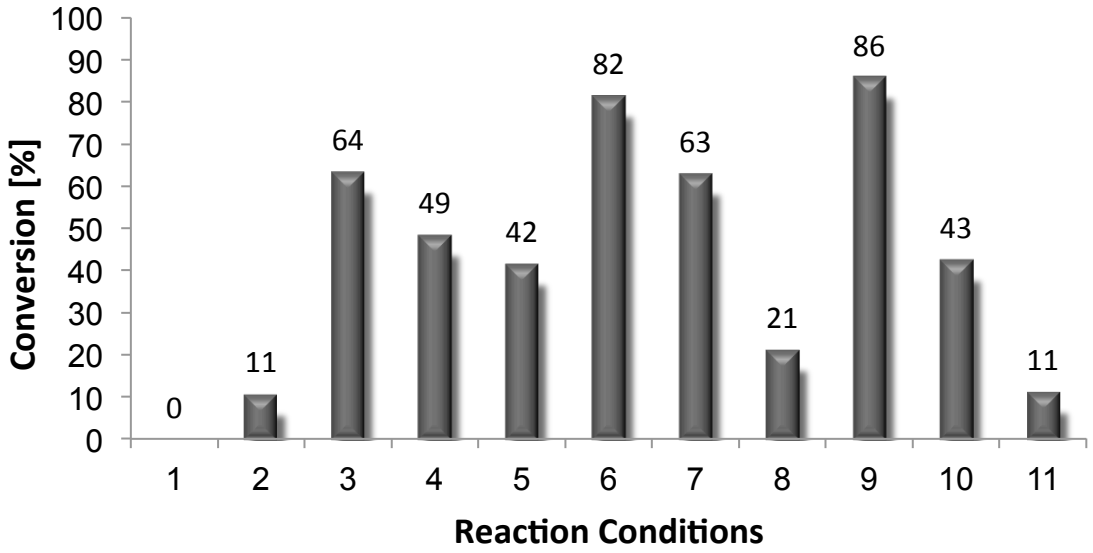


Broad screen of temperature, reaction time and the amount of Ni-Al alloy

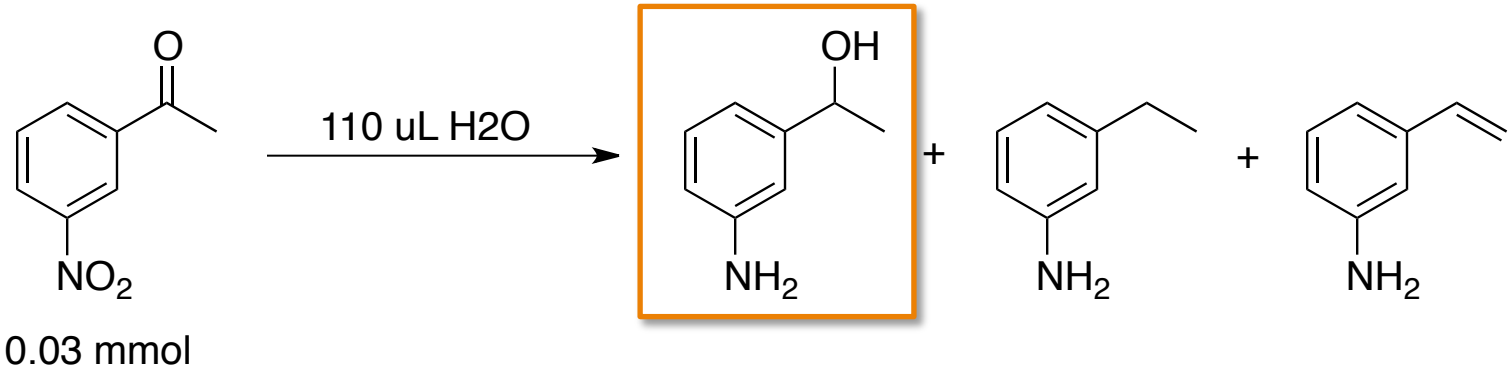


No.	Temp. (C)	Time (t)	Ni-Al alloy (mmol)
1	25	2	1.7
2	25	4	1.1
3	25	6	0.55
4	30	2.75	1.25
5	30	4.75	0.72
6	37	3.5	0.63
7	45	2	1.1
8	45	4	0.55
9	50	2.75	0.72
10	60	2	0.55
11	80	2	0.55

Ketone: 3-Nitroacetophenone



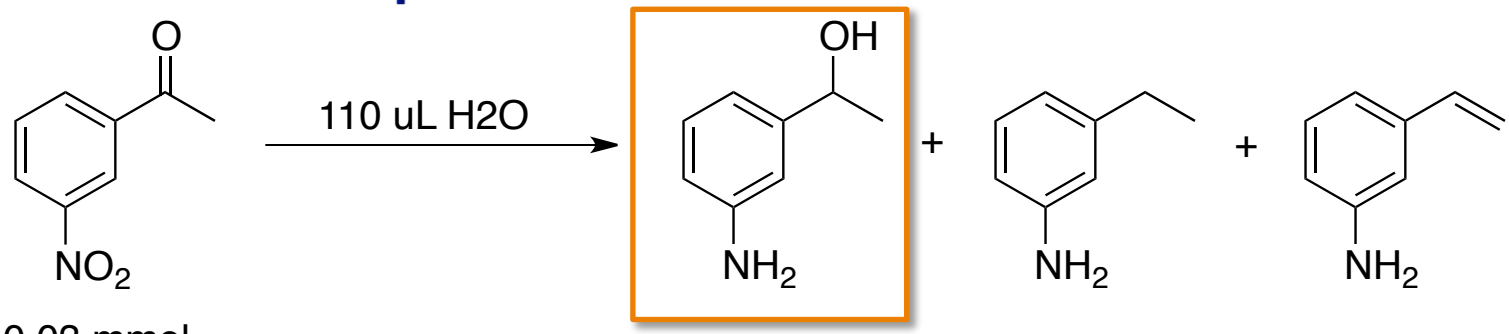
Effect of the amount of Ni-Al alloy, t, T, p



0.03 mmol

Pressure (kspi)	Temperature (h)	Ra-Ni alloy (mmol)	Time (h)	Conversion (%)	$Yield_{alcohol}$ (%)
40	35	0.25	8	75	70
40	**35**	**0.63**	**6**	**100**	**95**
40	35	1.25	7	77.7	65
40	35	1.67	7	69	65

Effect of the pressure

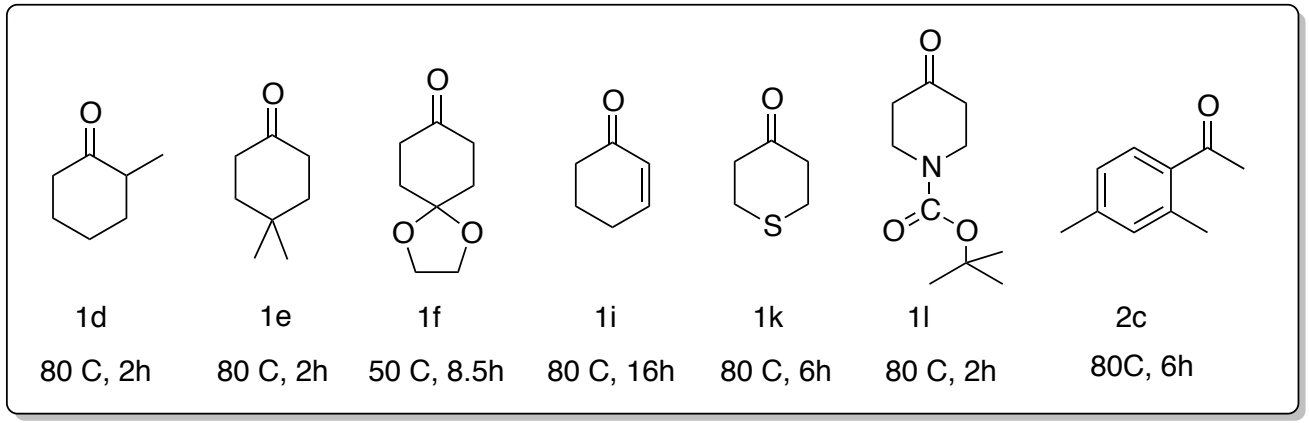


0.03 mmol

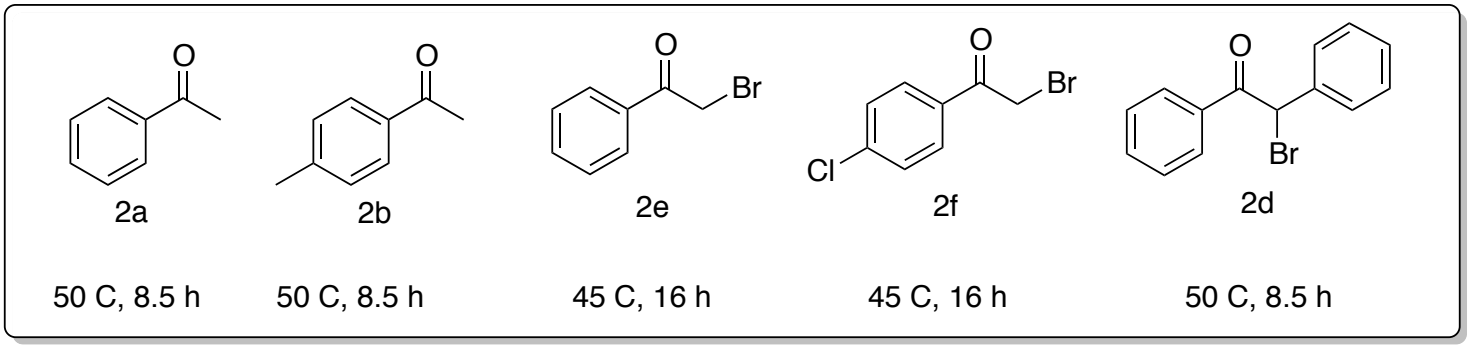
Pressure (kspi)	Temperature (h)	Ra-Ni alloy (mmol)	Time (h)	Conversion (%)	$Yield_{alcohol}$ (%)
5	35	0.25	6	99.5	1.1
5	50	0.25	6	74.2	69
5	80	0.25	6	98	65
20	35	0.25	6	0	0
20	50	0.25	6	49.6	44.9
20	80	0.25	6	100	72.1
40	**35**	**0.25**	**6**	**100**	**95**
40	50	0.25	6	37.1	0
40	80	0.25	6	100	o

Results regarding to alcohols

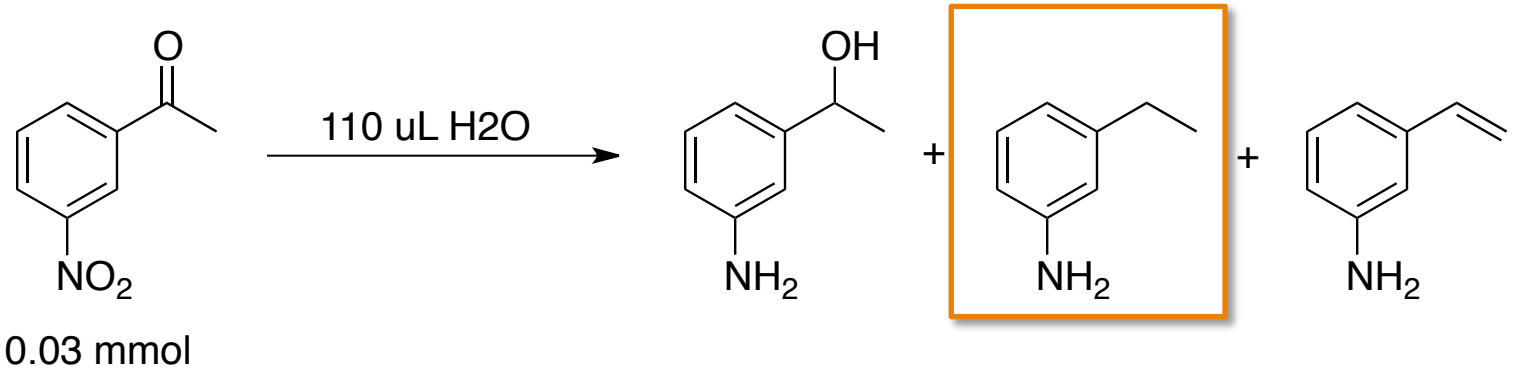
- > **95%** yield



- > **40-60%** yield



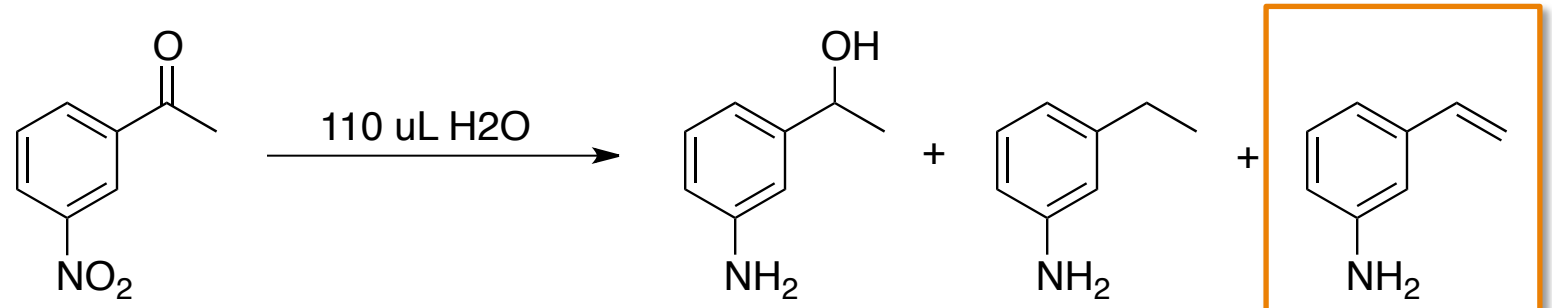
Effect of the amount of Ni-Al alloy, t, T, p



0.03 mmol

Pressure (kspi)	Temperature (h)	Ra-Ni alloy (mmol)	Time (h)	Conversion (%)	Yield$_{sat.}$ (%)
5	35	23	6	100	53

Effect of the amount of Ni-Al alloy, t, T, p



0.03 mmol

Pressure (kspi)	Temperature (h)	Ra-Ni alloy (mmol)	Time (h)	Conversion (%)	$Yield_{unsat.}$ (%)
40	30	23	16	100	96
40	50	23	8.5	100	93
20	45	23	16	100	92

Conclusion

- Development of "**green**" reduction method for broad variety of ketones
- Raney Ni-Al alloy, water, ketone & **high hydrostatic pressure**
- ***In situ*** generated **hydrogen** –> **remained** in the solution
- Corresponding porducts (alcohols, hydrocarbon, alkene) –> **good yield & selectivity**

Acknowledgements

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