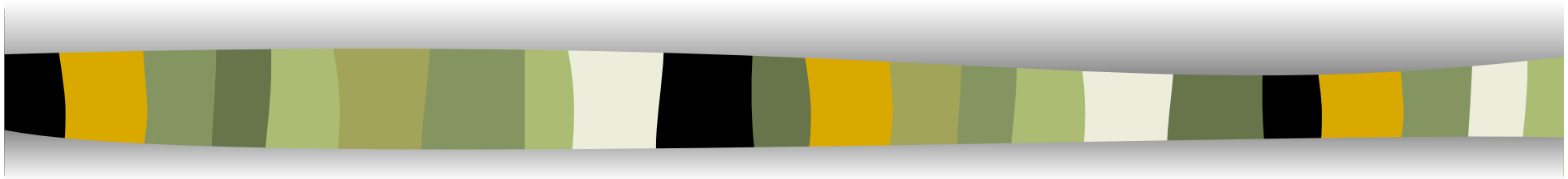
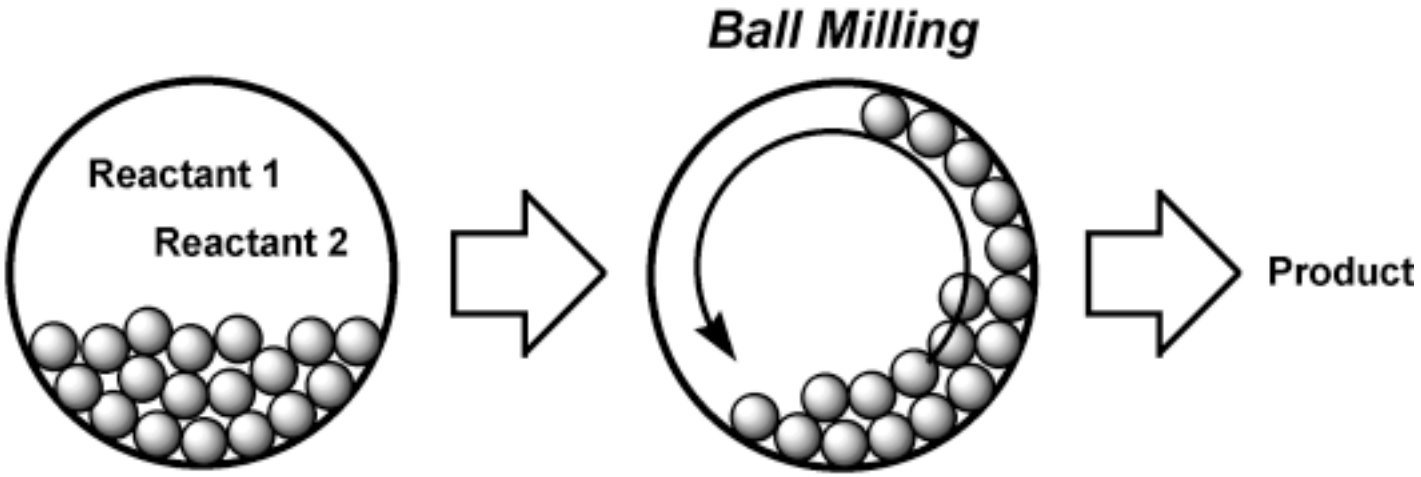
Ball Milling

An efficient and ecologically friendly synthetic approach

——— Jackie Ding





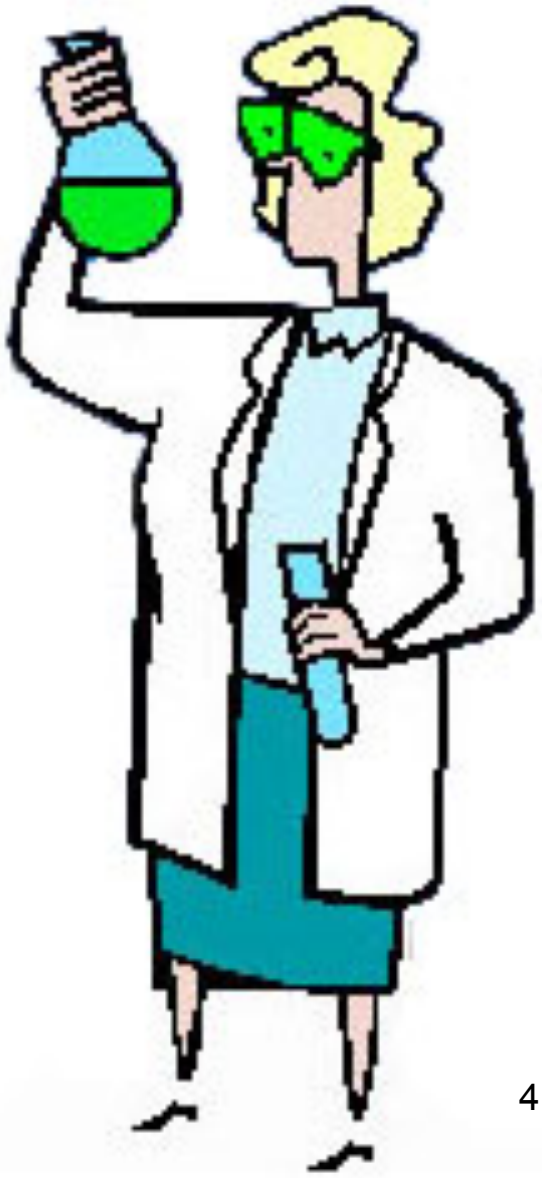
Content

- Environmental impacts of Solvent
- Ball milling – solvent free approach
- Application in organic synthesis
- Conclusion

The 12 Principles of Green Chemistry

- Prevention of waste
- Atom Economy
- Less Hazardous Chemical Syntheses
- Design Safer Chemicals
- Safer Solvents and Auxiliaries
- Design for Energy Efficiency
- Reduce Derivatives
- Use Renewable Feedstocks
- Catalysis
- Design for Degradation
- Real-time Analysis for Pollution Prevention
- Inherently Safer Chemistry for Accident Prevention

Do I need to use a solvent?



The best solvent is no solvent

- Alternative solvents:
  water
  supercritical CO_2
  ionic liquids

- Solventless Chemistry
  Mortar and pestle
  Ball milling

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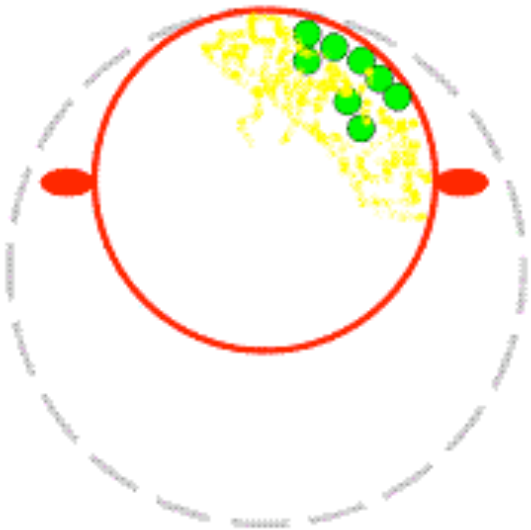
What is ball milling?

- A ball mill is a type of grinder used to grind materials into extremely fine powder.



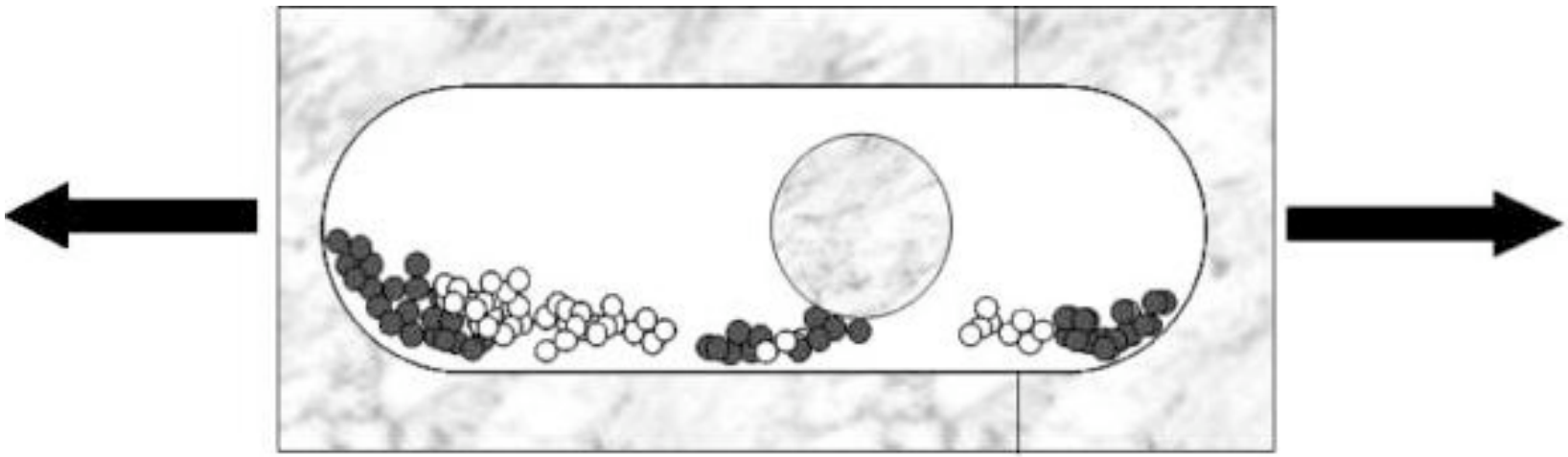
Major parameters for ball milling

- Temperature
- Size and Number of the balls
- Nature of the balls
- Rotation speed

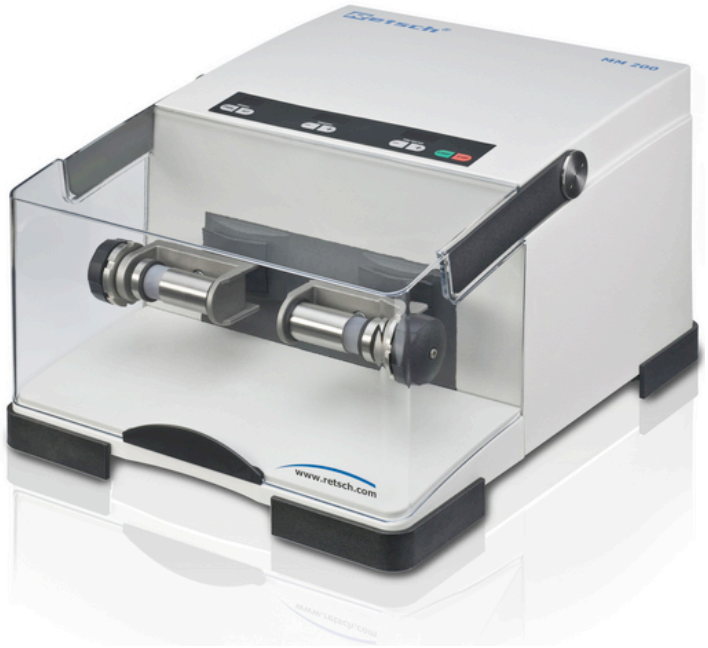
Types of Ball Mills

- Drum ball mills
- Jet-mills
- Bead-mills
- Horizontal rotary ball mills
- **Vibration ball mills**
- **Planetary ball mills**

Vibration Mills

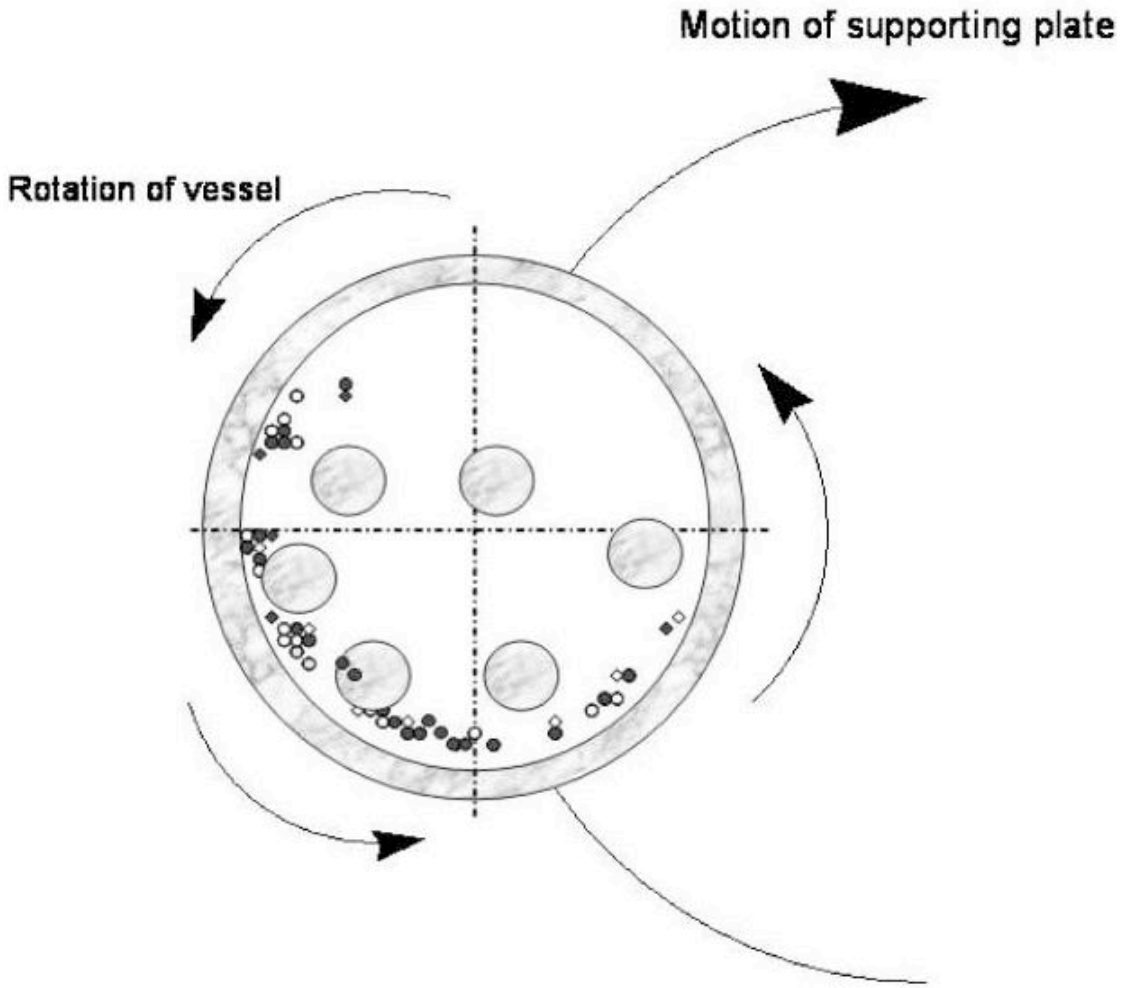


Mixer Mill MM 400



- Feed material: hard, medium-hard, soft, brittle, elastic, fibrous
- Material feed size: ≤ 8 mm
- Final fineness: ~ 5 µm
- Setting of vibrational frequency: digital, 3 - 30 Hz (180 - 1800 min^{-1})

Planetary Mills



Planetary Ball Mill PM 400

- Feed material: soft, hard, brittle, fibrous (dry or wet);
- Material feed size: < 10 mm;
- Final fineness < 1 µm;
- No. of grinding stations: 4 / 2

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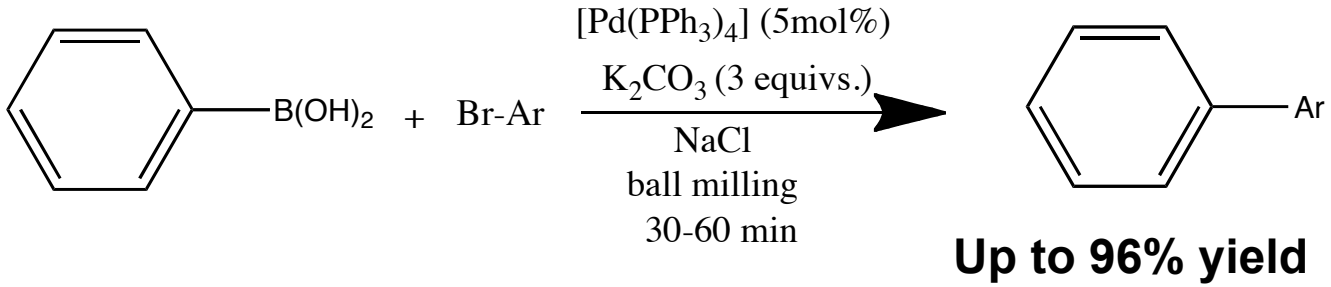
Application in Organic Synthesis

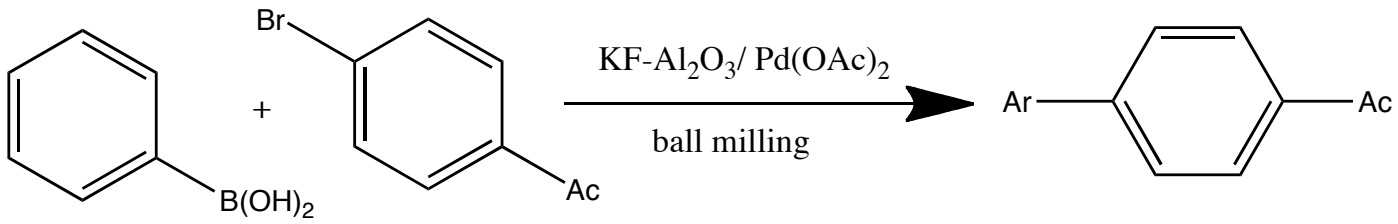
- Aldol Condensations
- Knoevenagel Condensations
- Baylis-Hillman Reaction
- Michael Reaction
- Wittig Reaction
- Fullerene Cycloadditions
- Suzuki Reaction
- Heck-Jeffery Reaction
- Radical Additions Mediated by Mn (III)
- Etc.

Suzuki reaction



Up to 96% yield

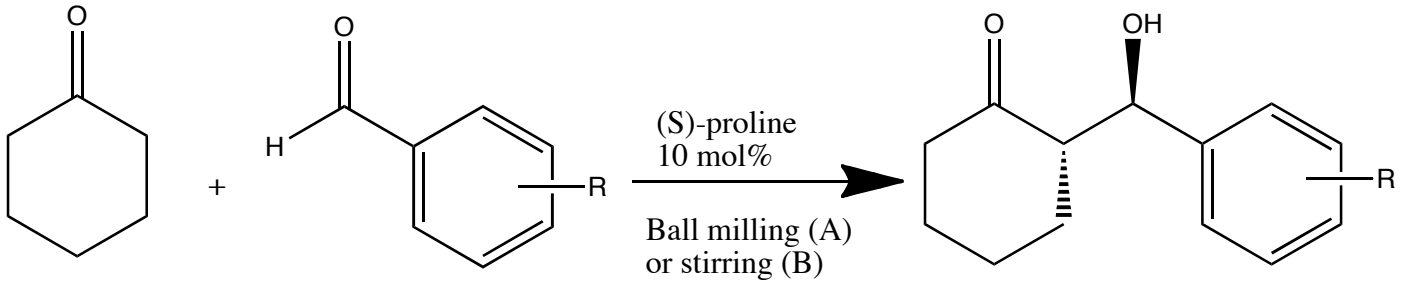
S. F. Nielsen, O. Axelsson, *Synth. Commun.* 2000, 30, 3501.



Entry	Rpm	T (min)	Yield%
1	400	10	**92**
2	800	5	**94**

Franziska Schneider, *Org. Proc. Res. & Develop.*, 2009, 13,44

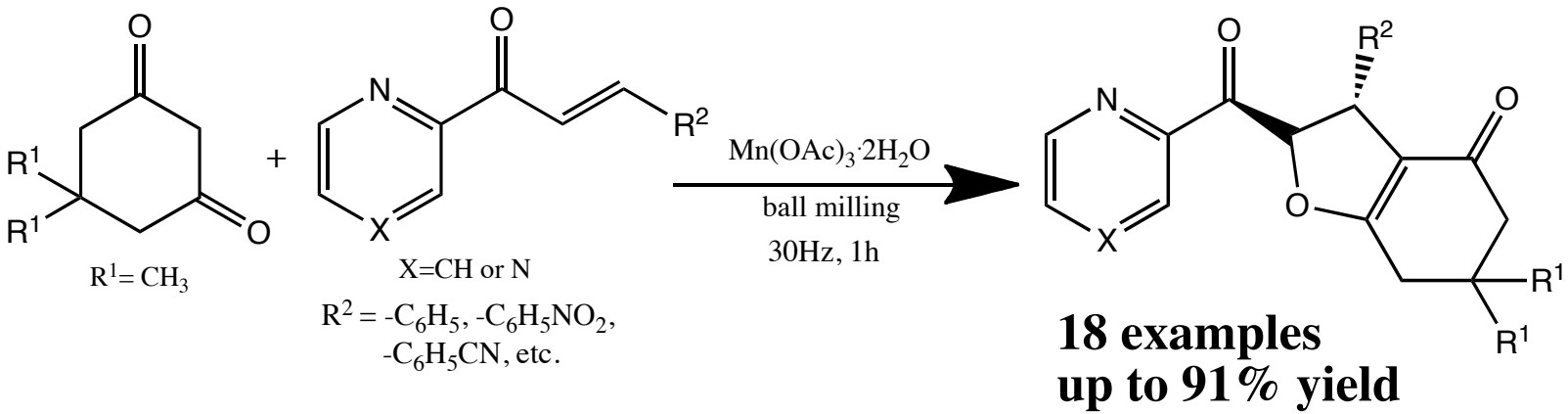
Aldol Condensation



Entry	R=	Method	*t*/h	Yield%	*anti/syn*	ee%
1	4-NO_2	A	5.5	99	89:11	94
2	4-NO_2	B	24	95	89:11	94
3	3-NO_2	A	7	94	88:12	>99
4	3-NO_2	B	16	89	82:18	98
5	2-NO_2	A	7	97	93:7	97
6	2-NO_2	B	36	89	91:9	97

B. Rodr´ıguez, *Angew. Chem., Int. Ed.,* 2006, 45, 6924

Oxidation



Conventional heating in organic solvent:

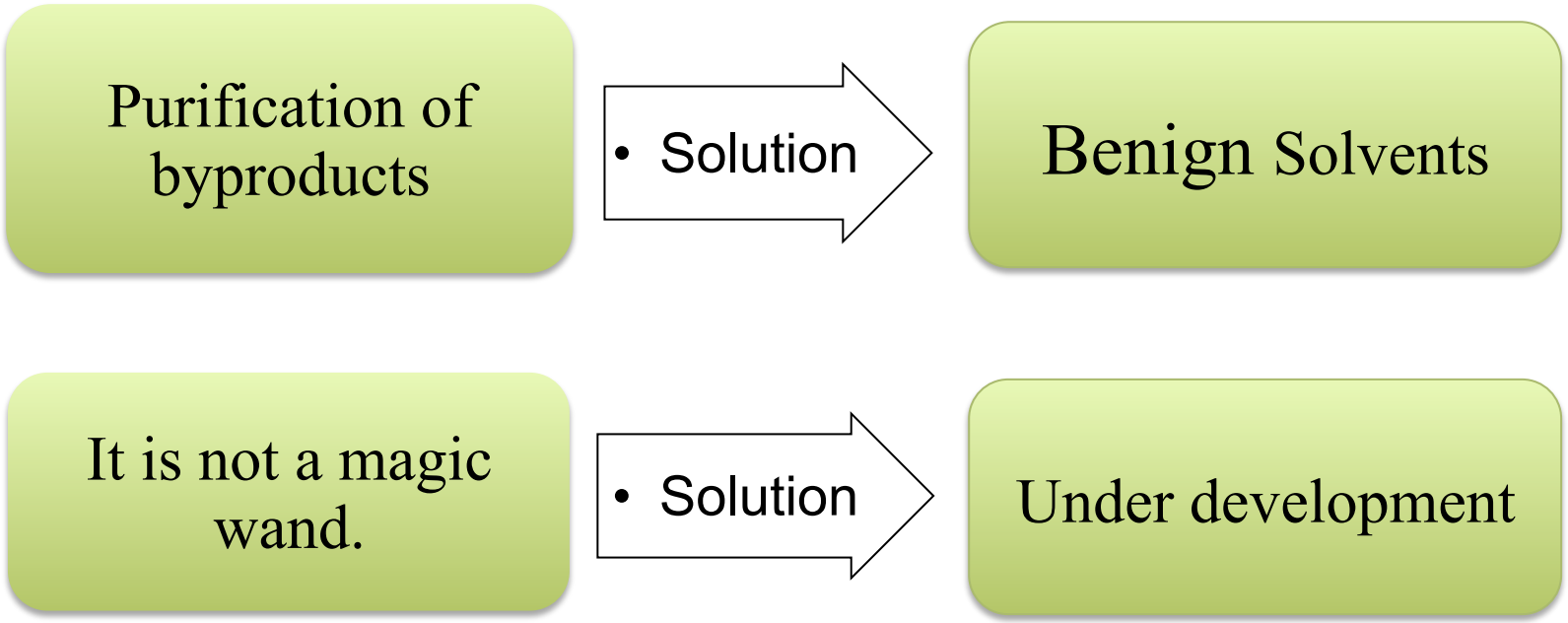
a. Acetic acid, 80°C, argon atmosphere, yield **32%**
b. Ethanol, refluxing temperature for 12h, yield **48%**

Guan-Wu Wang, *J. Org. Chem*. 73, 7088 (2008).

Other applications of ball milling

- Fine particles
- Inorganic solids

Drawbacks of ball milling



Conclusion

- Ball milling should be considered as a potentially attractive solution for solvent-free synthesis.

Reference

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Thank
You