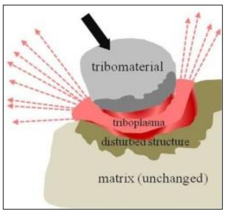
waste-free mechanochemical syntheses without auxiliaries

solid-state ☼ 100% yield ☼ no solvents

more than 1000 known quantitative waste-free solid-state reactions since 1984

G. Kaupp, *Cryst. Eng. Comm*, 2006, **8**, 794–804; G. Kaupp, *Top. Curr. Chem*., 2005, **254**, 95–183;
G. Kaupp et al., *Chem. Eng. Sci.*, 2002, **57**, 763-765; Ren et al.. Adv. Powder. Metall. Mat. 2003, 216-222



Mechanochemistry in mills - a comparison

Industrial mills of different types are in practical use for a number of commercial applications. Among these, vibration mills have to move the whole mass of the grinding chamber. This produces high noise levels and environmental vibrations; it limits the sizes and the speed of the milling tools. Furthermore, they are almost impossible to be operated under controlled condition of atmosphere or closed circuit. The same is valid for simple (drum-) ball mills with a rotating vessel. Jet mills use large streams of air or inert gas, which limits their use in reactive milling and the absence of grinding media excludes significant kinetic effects. Horizontal or vertical bead mills do not exhibit a significant kinetic impact since no high-level relative acceleration of the grinding tools occurs. They experience shear- and friction effects but not collision. Planetary ball mills and shaker mills are limited to laboratory size. The most suitable choice is horizontal rotary ball mills (Simoloyer®) with cooling/heating mantle that can be operated in dry milling at high relative velocity of the grinding media (up to 16 m·s-1) that cannot be reached by the other technical ball mills. Furthermore, they run under controlled conditions like vacuum, inert gas or in closed circuits. The systems are presently available from 0.5 to 400 l grinding chamber capacity, and larger volumes seem to be possible. They are already in wide industrial use for mechanical alloying of different metals and/or ceramics and production of nanocrystalline metal hydrides, due to an intensive grinding effect at low energy costs (e.g. 600 W at 1200 rpm of the 2 l version) and short process times with lowest contamination of the processed powders by the milling tools, since the process is based on the collision of grinding media rather than on shear and friction (extract from: G. Kaupp, Cryst. Eng. Comm, 2006, ***8****, 794–804).*

Safety remarks

- ⚠ Gas–solid reactions may be highly vigorous if finely ground crystals are applied. Do not apply preceding or supporting milling unless the reaction is incomplete due to surface passivation.
- ⚠ Do not mill explosive solids, as these might explode upon the heavy shocks despite the presence of the steel balls with high heat capacity
- ⚠ Do not mill under enclosed air but under vacuum or inert gas if hydrogen or methane or other burning gas is a reaction product in order to avoid explosive gas mixtures.
- ⚠ Do not use milling for oxidations of highly reducing solid materials with oxidizing gases such as nitrogen dioxide or oxygen that might become violent with micronized dusts.

Exemplary successful quantitative reactions

solid-gas

- alkali alcoholates and CO_2
  - ⇨ sodium methanolate, sodium ethanolate, potassium tert-butanolate

Knoevenagel condensations

- *p*-hydroxybenzaldehyde and barbituric acid / N,N'-dimethylbarbituric acid

Condensation of amines

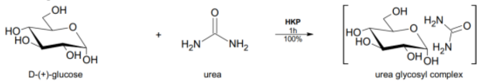
- solid derivatives of aniline and benzaldehyde
- *o*-phenylenediamine and benzyls
- 1,3-diketonbes and solid aniline derivatives
- (L)-proline / (L)-cysteine and paraformaldehyde
- imidazole/benzimidazole and paraformaldehyde
- (L)-proline and ninhydrin
- pyrazolidinone with solid derivatives of benzaldehyde
  - ⇨ Nitro-, Chloro-, Bromobenzaldehyde
- o-phenylenediamine dihydrochloride and degasseod frozen acetone and subsequent NaOH
- gaseous methylamine or ethylamine with solid benzaldehydes
- tetrachlorophthalic anhydride and ethylamine (ring opening)
- solid aromatic amines and phthalic anhydride (ring opening)
- solid thiohydantoins and methylamine (ring opening)

Inorganic syntheses

- nitrogen dioxide with sodium nitrite
- copper cyanide and sodium cyanide
- metals and sulphur
  - ⇨ Cu, Fe
- lead oxide and chromium oxide or titanium oxide

complexations

- glucose and urea



Heterocyclic syntheses

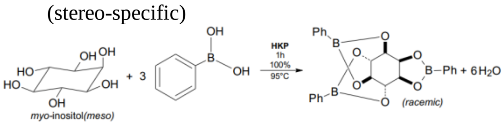
- Phenacylbromide or chloroacetyl substituted heterocyclics to 2-aminothiazoles

salt formation

- amino acids and gaseous HCl
  - ⇨ (L)-phenylalanine, (D)-penicillamine, (DL)-penicillamine, (L)-cysteine, (L)-leucine, (L)-proline, (DL)-tyrosine, (L)-histidine
- *o*-phenylenediamine and gaseous HCl
- (L)-(+)-tartaric acid and sodium hydrogencarbonate or sodium carbonate
- furan-2-carboxylic acid and ammonia
- 2-mercaptobenzothiazole and methylamine

Further organic reactions

- bromine and cholesterol
- bromine and thetraphenylethene
- (D)-mannitol or myo-inositol and phenylboronic acid (stereo-specific)



- aldehydes and sodium boron hydride
- dioxin and silicon dioxide

…and many more