A Quantitative Understanding of the Water Effect on the Amine Catalyzed Aldol Reaction

Anton De Vylder[1], Jeroen Lauwaert[2], Maarten K. Sabbe[1,2], Jeriffa De Clercq[2], Pascal van der Voort[3], Joris W. Thybaut[1]

[1]Laboratory for Chemical Technology (LCT)

[2]Industrial Catalysis and Adsorption Technology (INCAT)

[3]Center for Ordered Materials, Organometallics and Catalysis (COMOC)

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

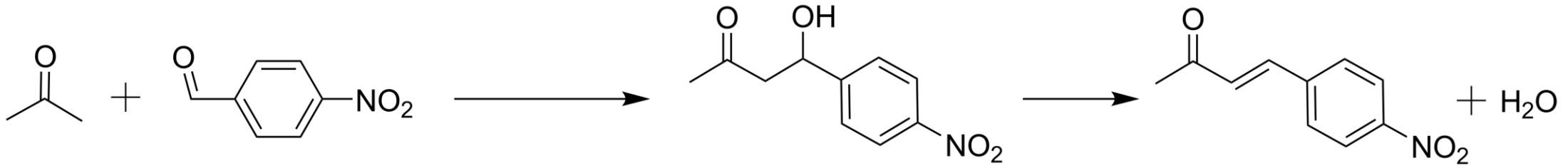
Center for Ordered Materials, Organometallics & Catalysis

INCAT

Industrial Catalysis and Adsorption Technology

Amino(-acid) catalyzed aldol reaction

carbon-carbon coupling reaction between two carbonyl species



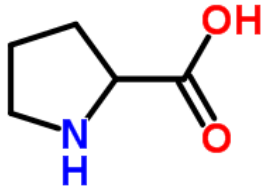
aldol adduct

enone product

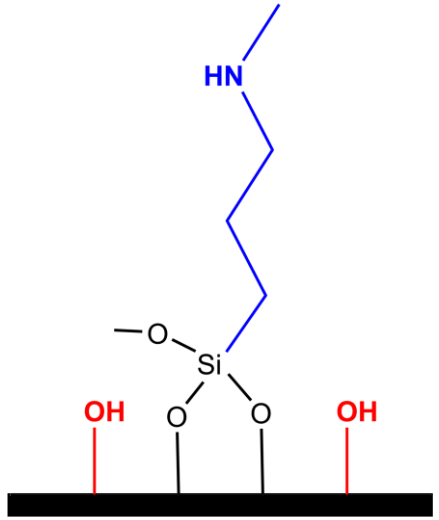
homogeneous

- NaOH
- $Ca(OH)_2$
- Na_2CO_3

L-proline



heterogeneous

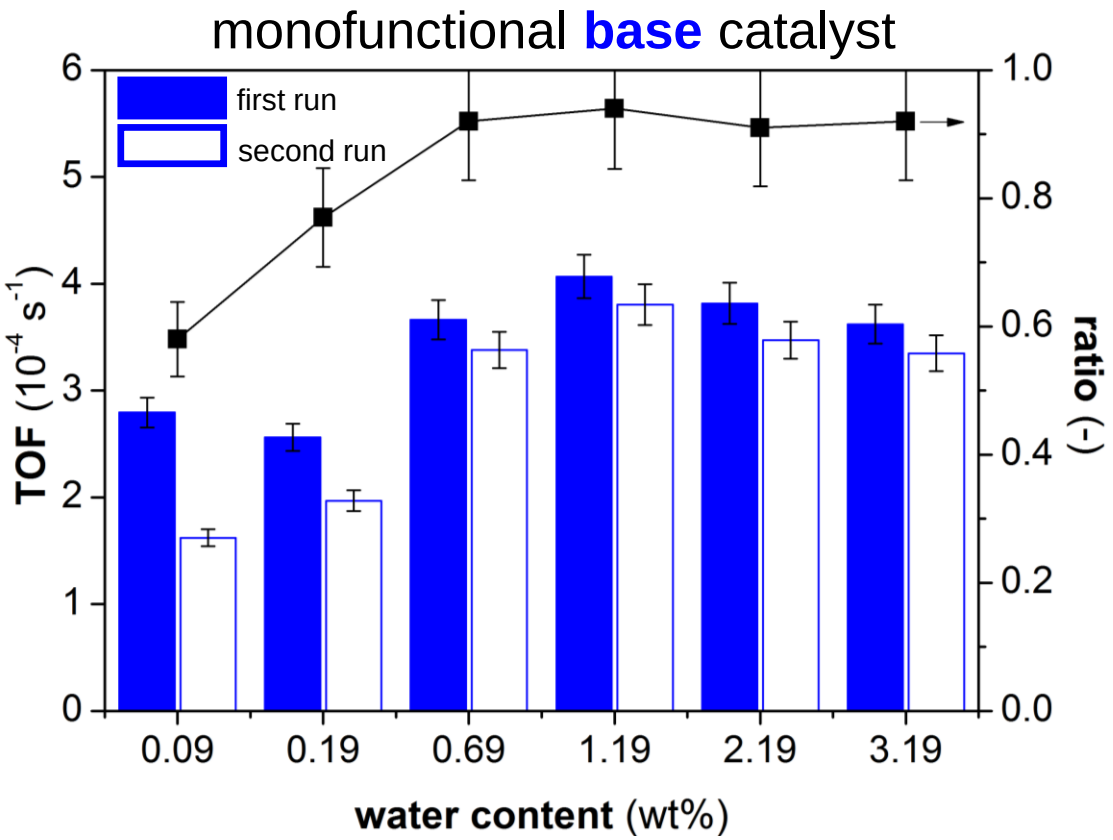


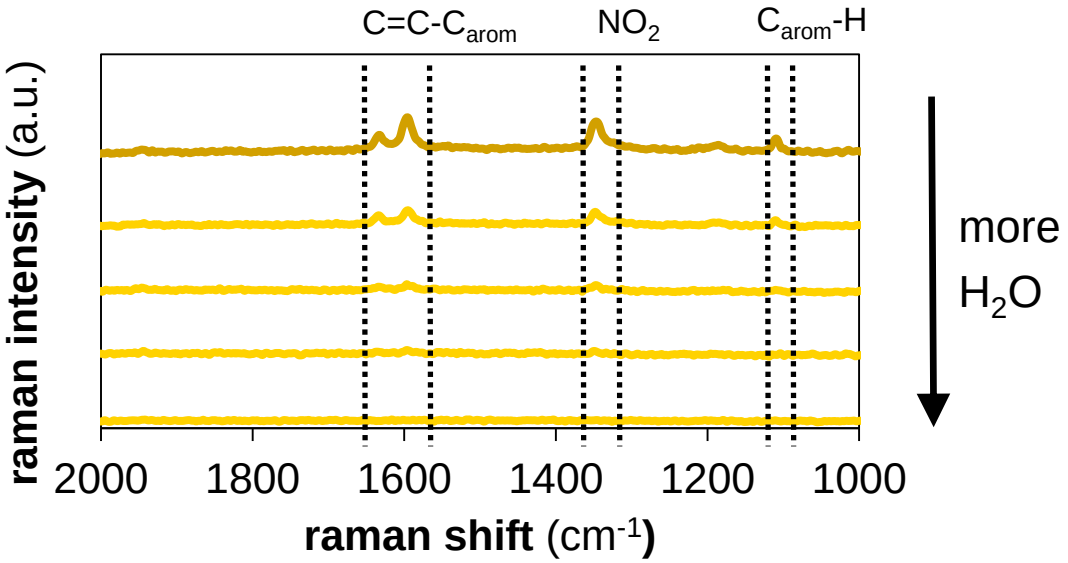
acid-base cooperativity

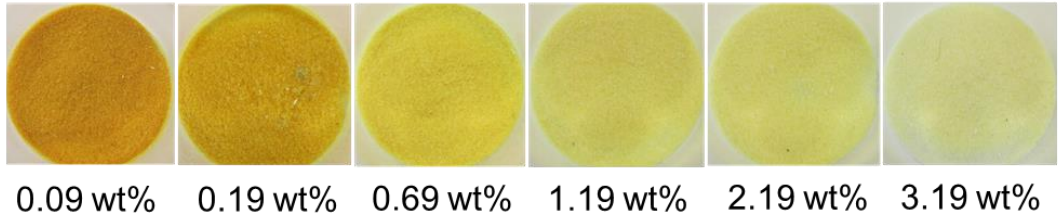
GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

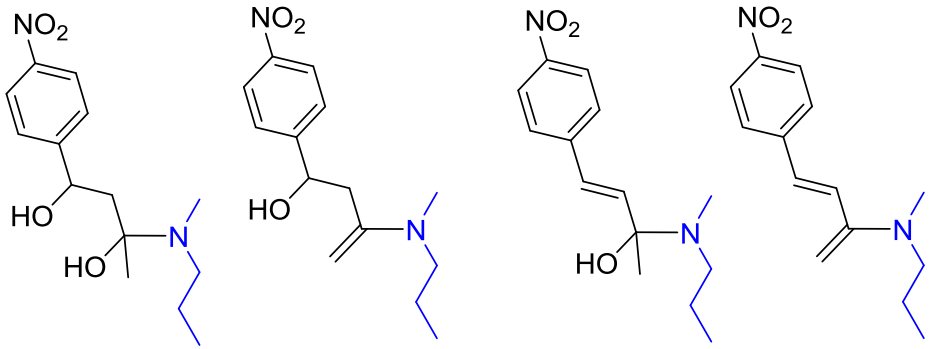
Previous experimental work[1]: the effect of water







T = 55 °C, 0.45 g 4-nitrobenzaldehyde, **50 vol% acetone 50 vol% DMSO**, 0.20 g methyl-4-nitrobenzoate, 0.5 g to 3.0 g water. Water concentrations determined with Karl-Fischer.



GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

1) De Vylder A, et al. J. Catal. 361. p.51-61 **2018**

Outline

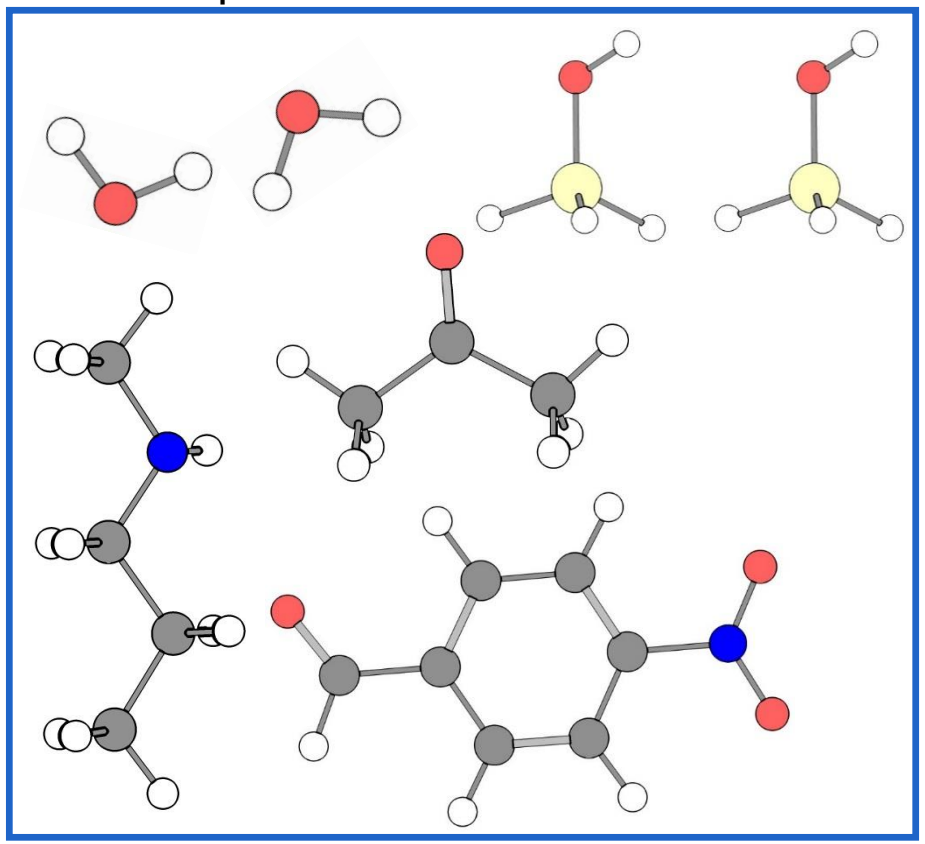
- Introduction
- The effect of water on site-blocking species in the amine catalyzed aldol reaction
- Silanol groups as promotor for the amine catalyzed aldol reaction
- Conclusions

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Construction of a computational model

p = 1 atm T = 328.15 K



50 vol% DMSO as solvent

50 vol% acetone

- level of theory: **CBS-QB3** (tight)
- active site represented as homogeneous **N-methylaminopropane**
- reagent 1: **acetone**
- reagent 2: **4-nitrobenzaldehyde**
- zero, one or two **water** molecules explicitly incorporated
- zero, one or two **silanol** groups incorporated
- removed contributions of external rotation and translation to the partition functions for surface species
- bulk solvation with COSMO-RS: $\mathbf{\Delta G_{solv,Henry}}$ (mol/L)
- correction standard state gas (1 atm) → liquid (1 mol/L)

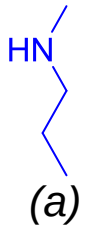
$$\Delta G_S^l = \Delta G_S^g + \Delta G^{l \to g}$$

$$\Delta G^{l \to g} = RT\ln\left(\frac{V^l}{V^g}\right) = 7.95 \text{ kJ/mol}$$

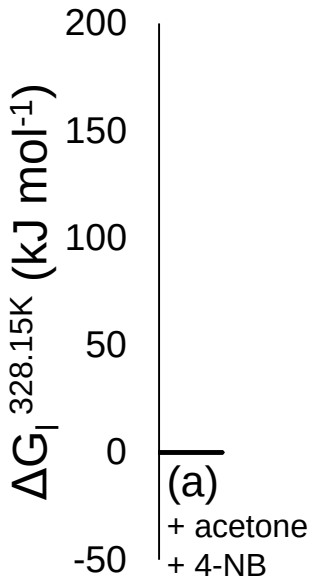
GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water



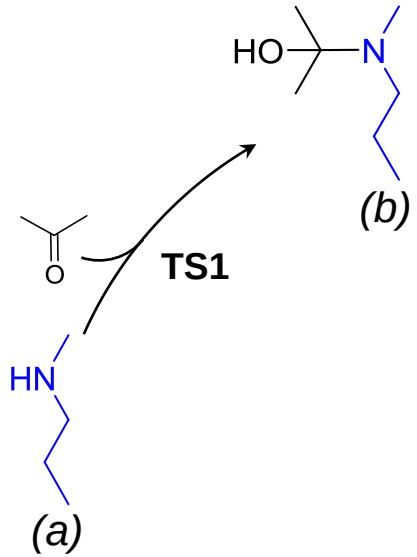
(a)

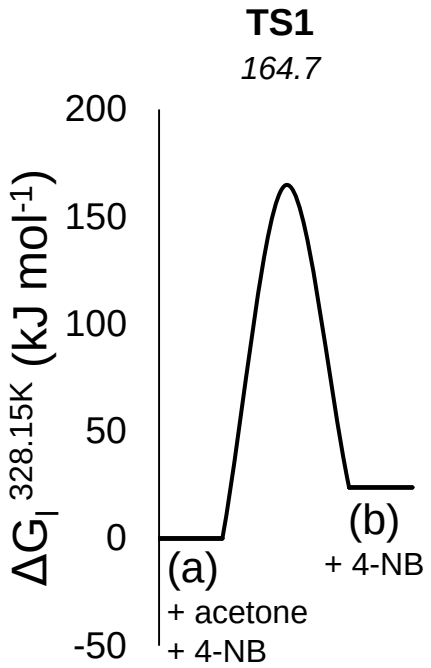


GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water

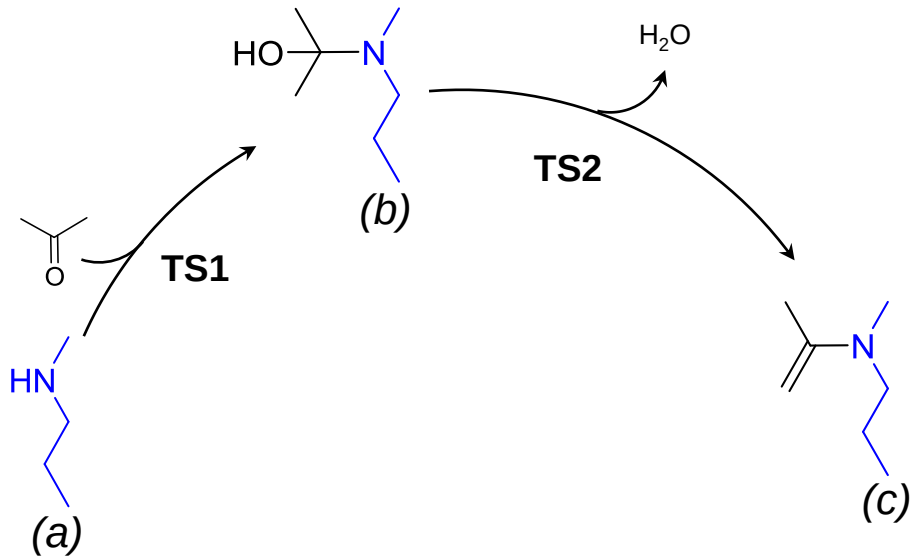


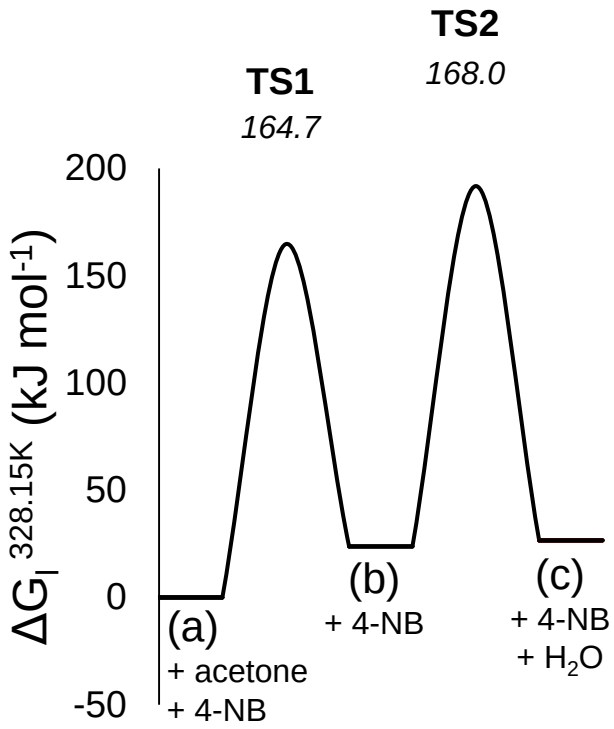


GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water

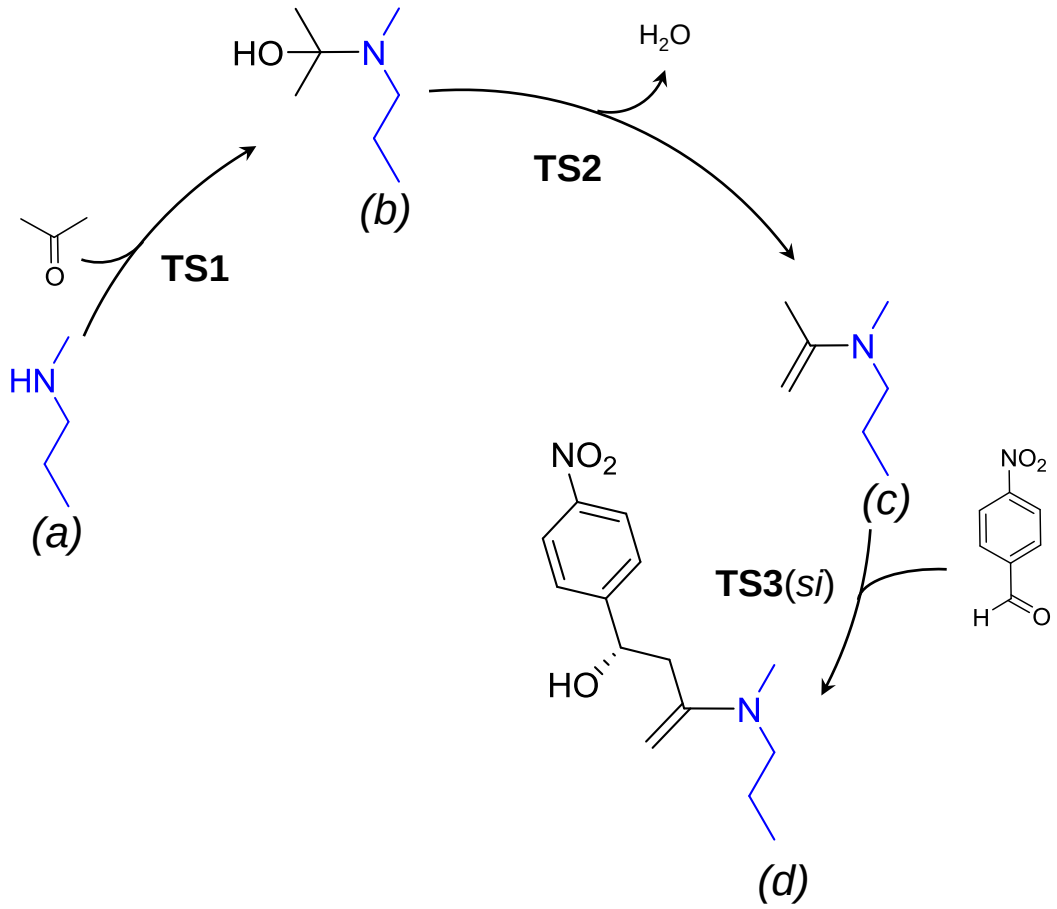


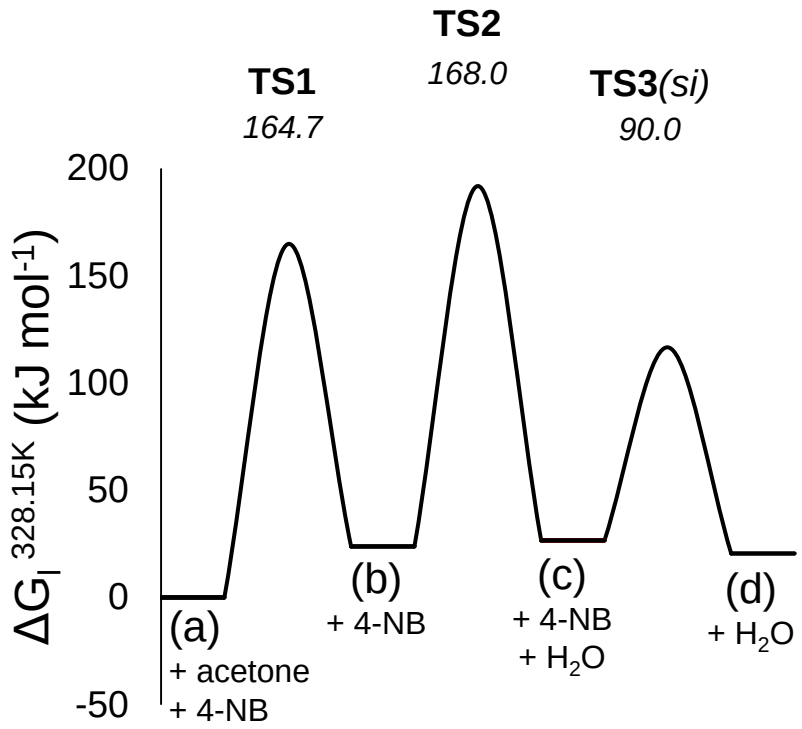


GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water

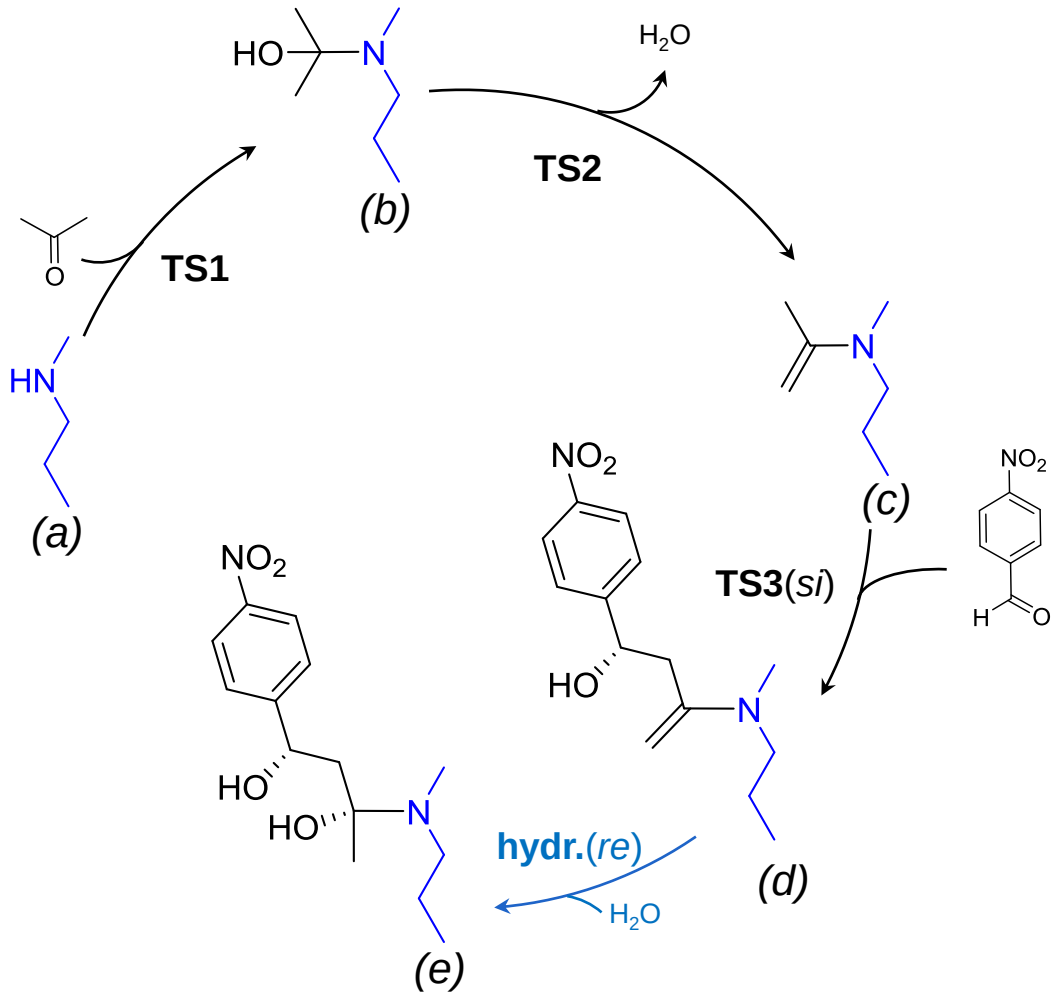


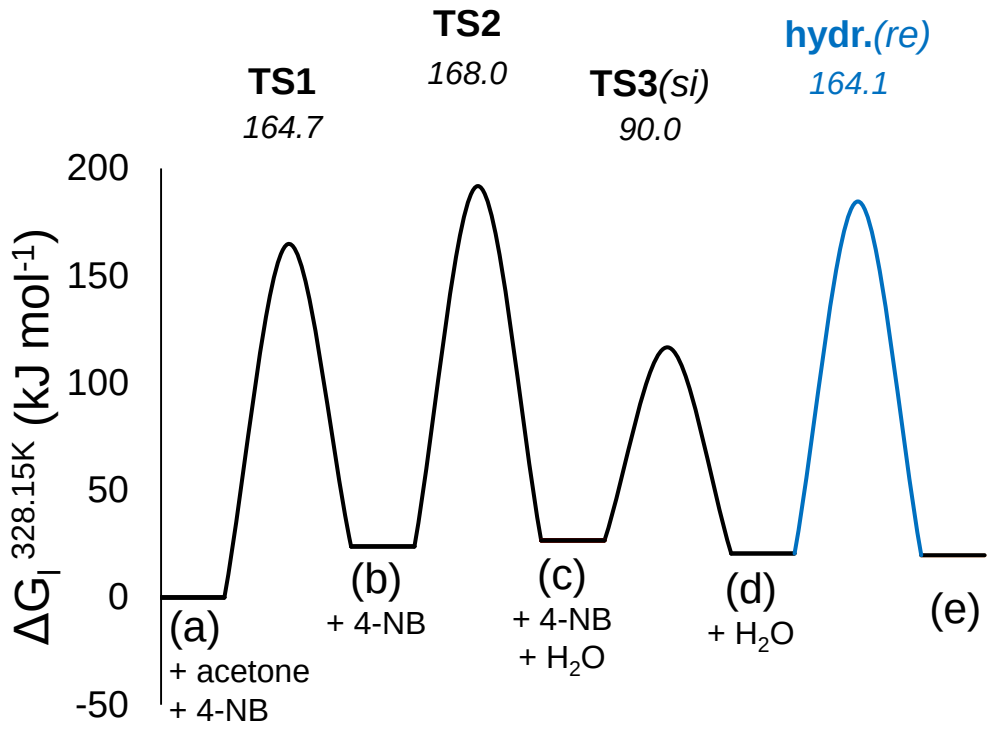


GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water

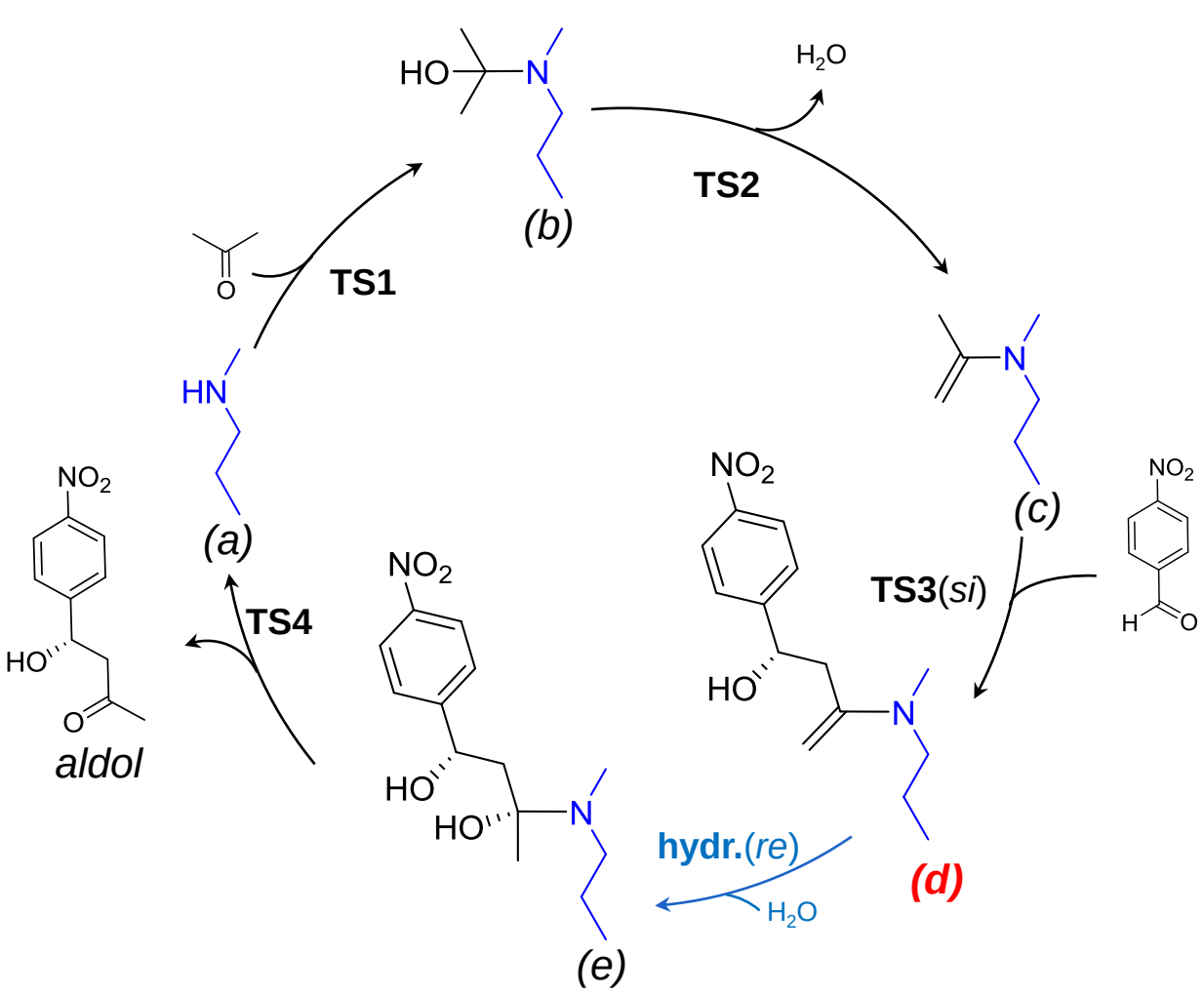


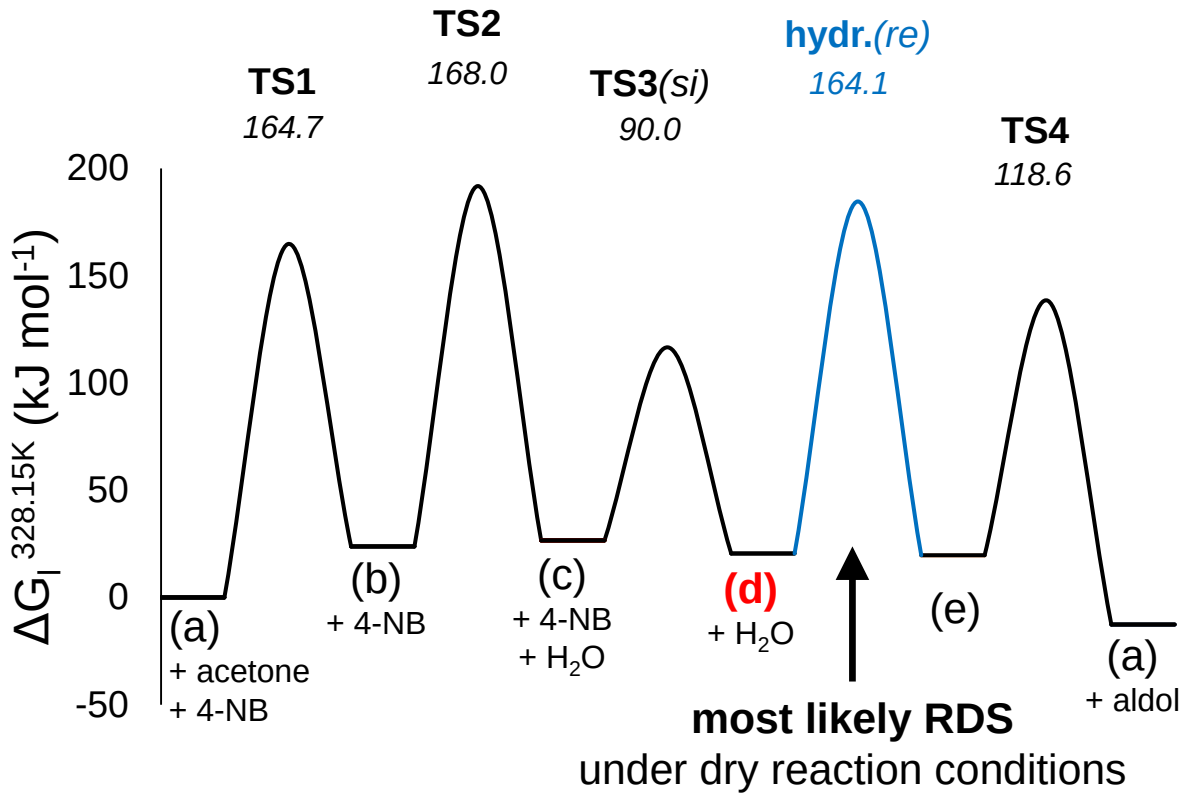


GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water

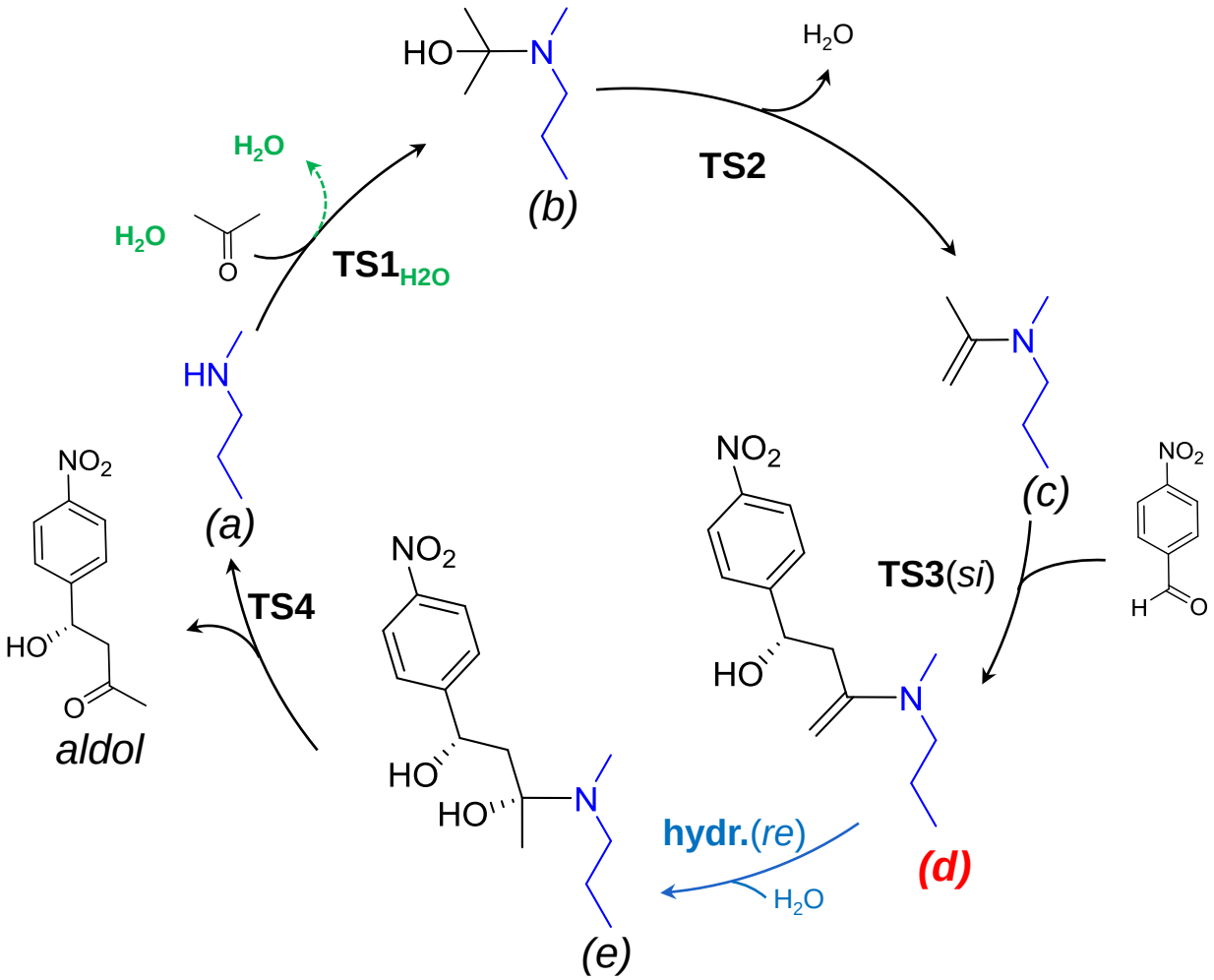


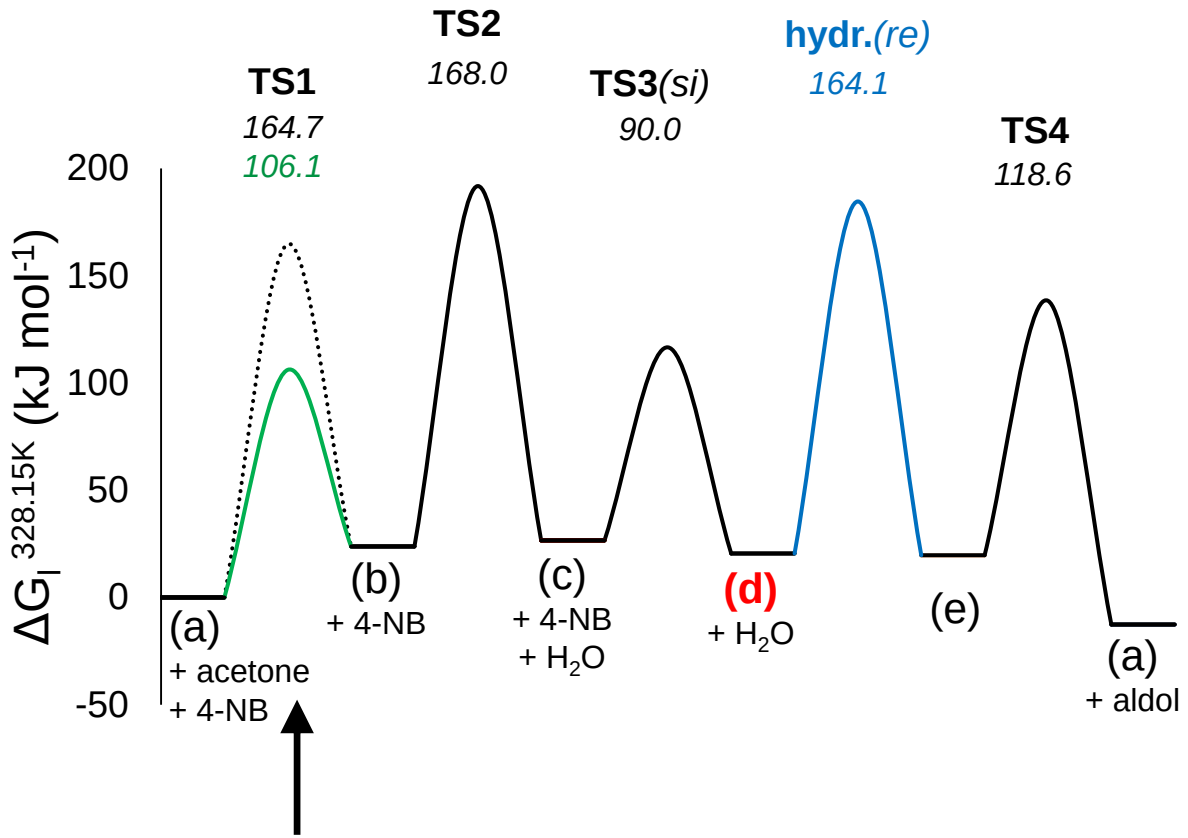


GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water



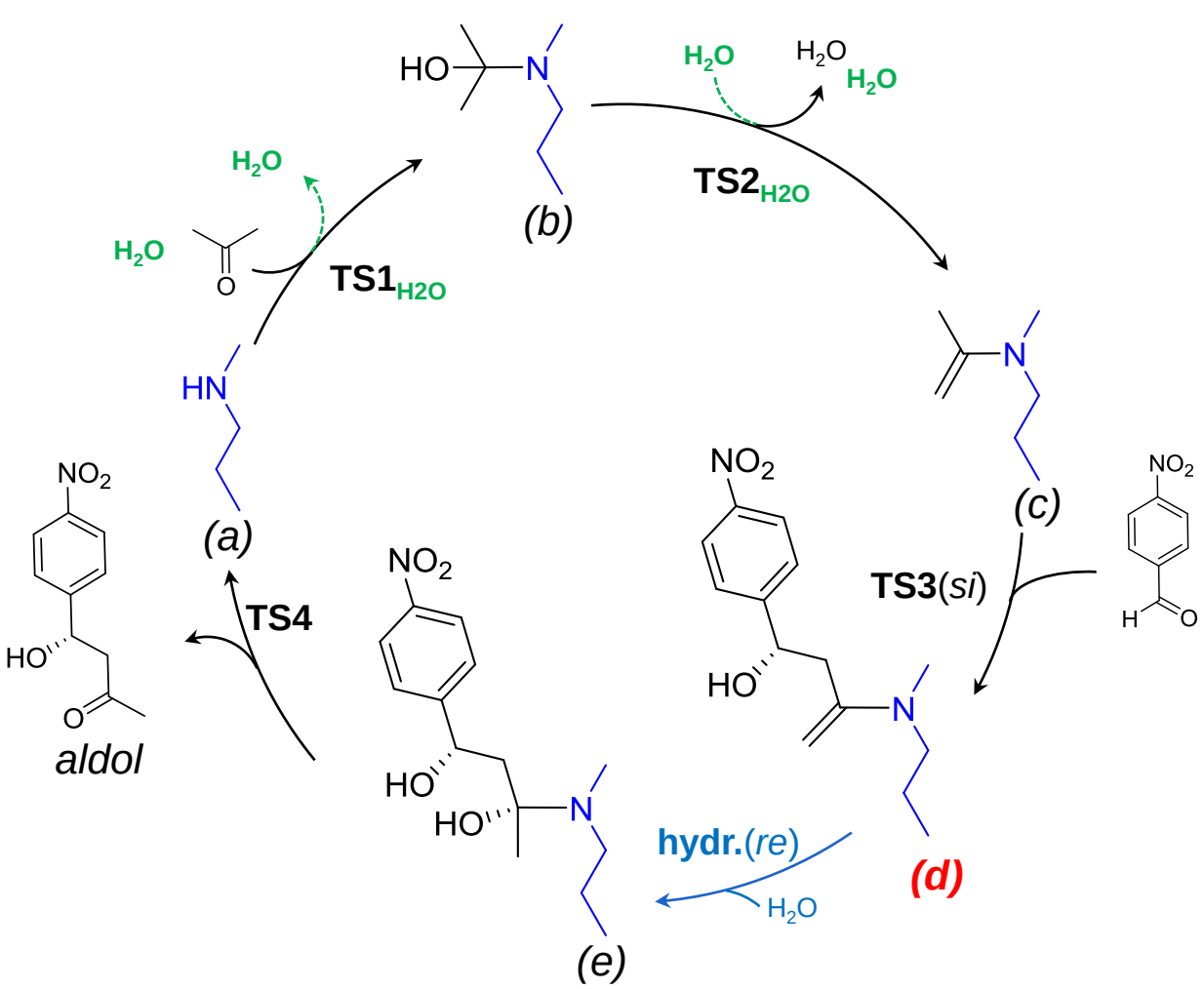


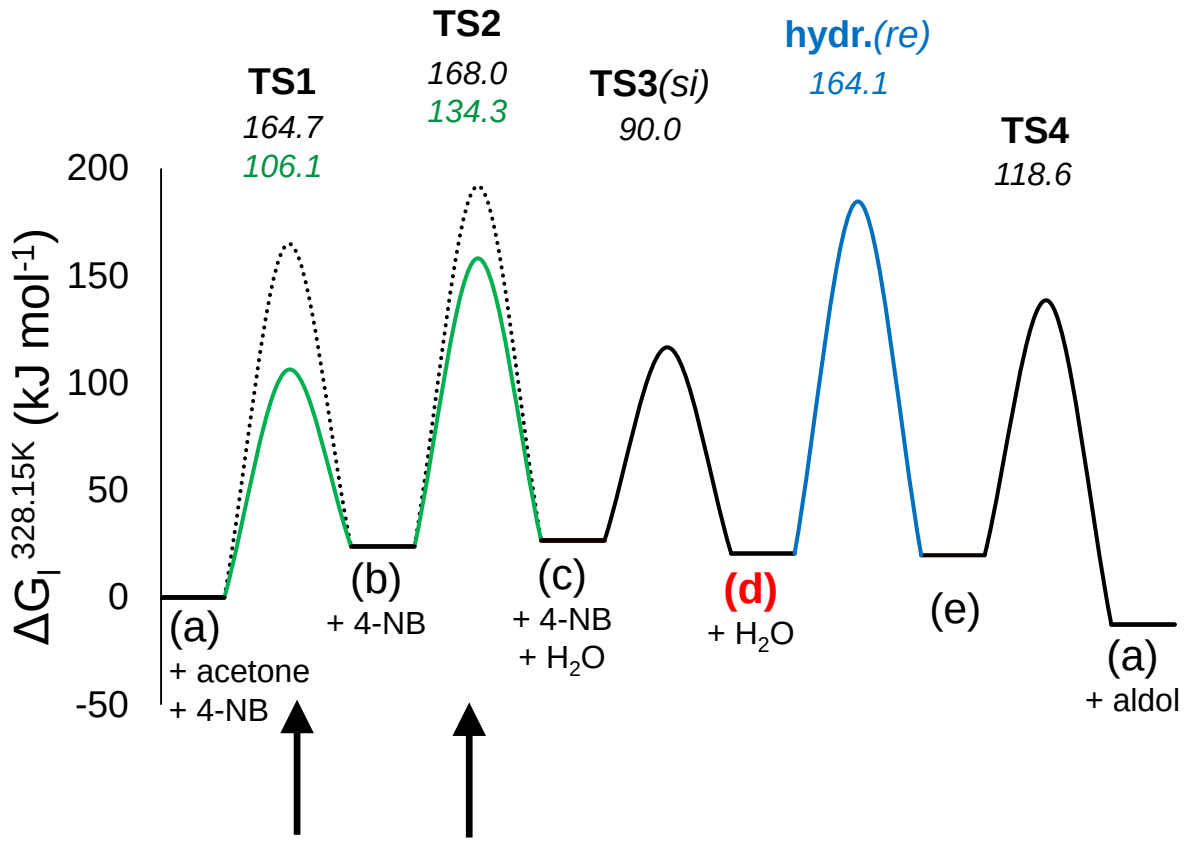
lower barrier due to water promoting the proton transfer

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water



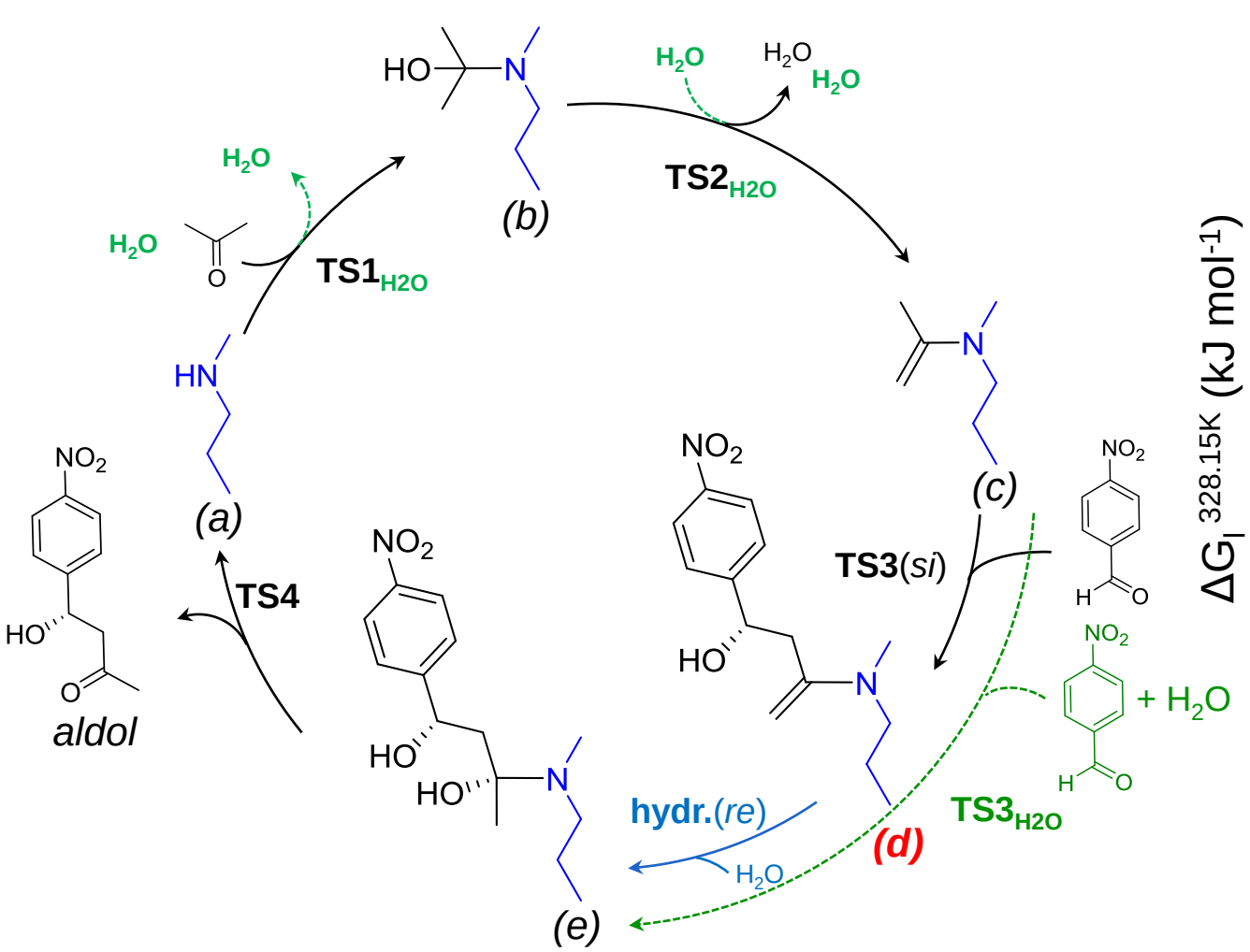


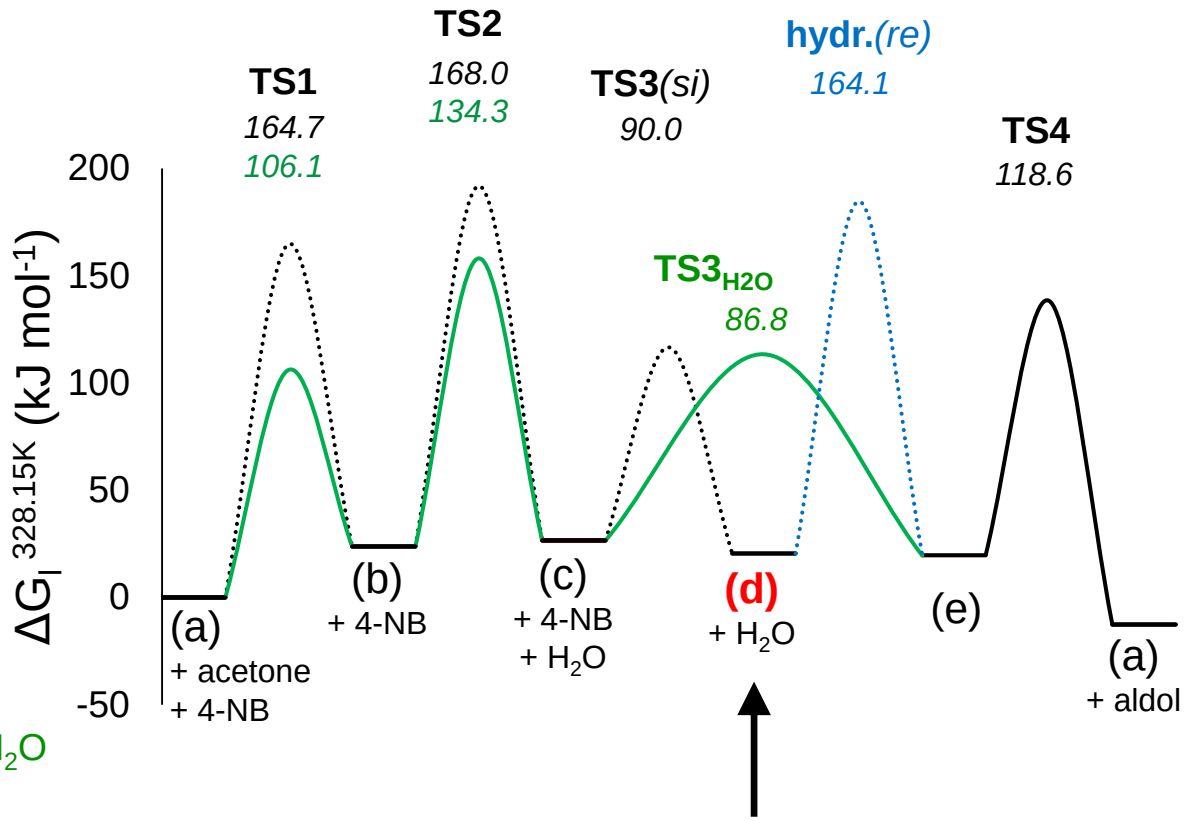
lower barrier due to water promoting the proton transfer

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water



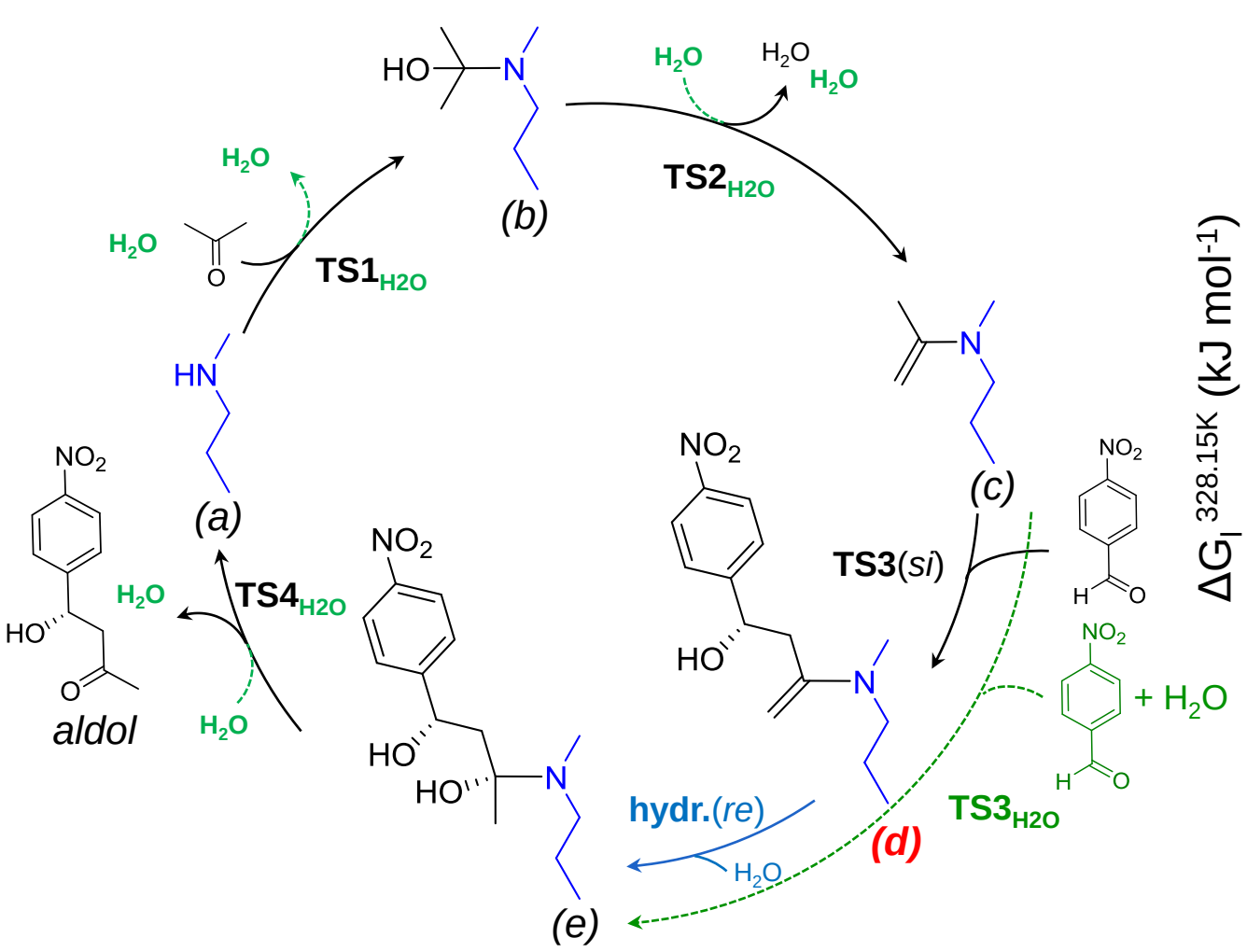


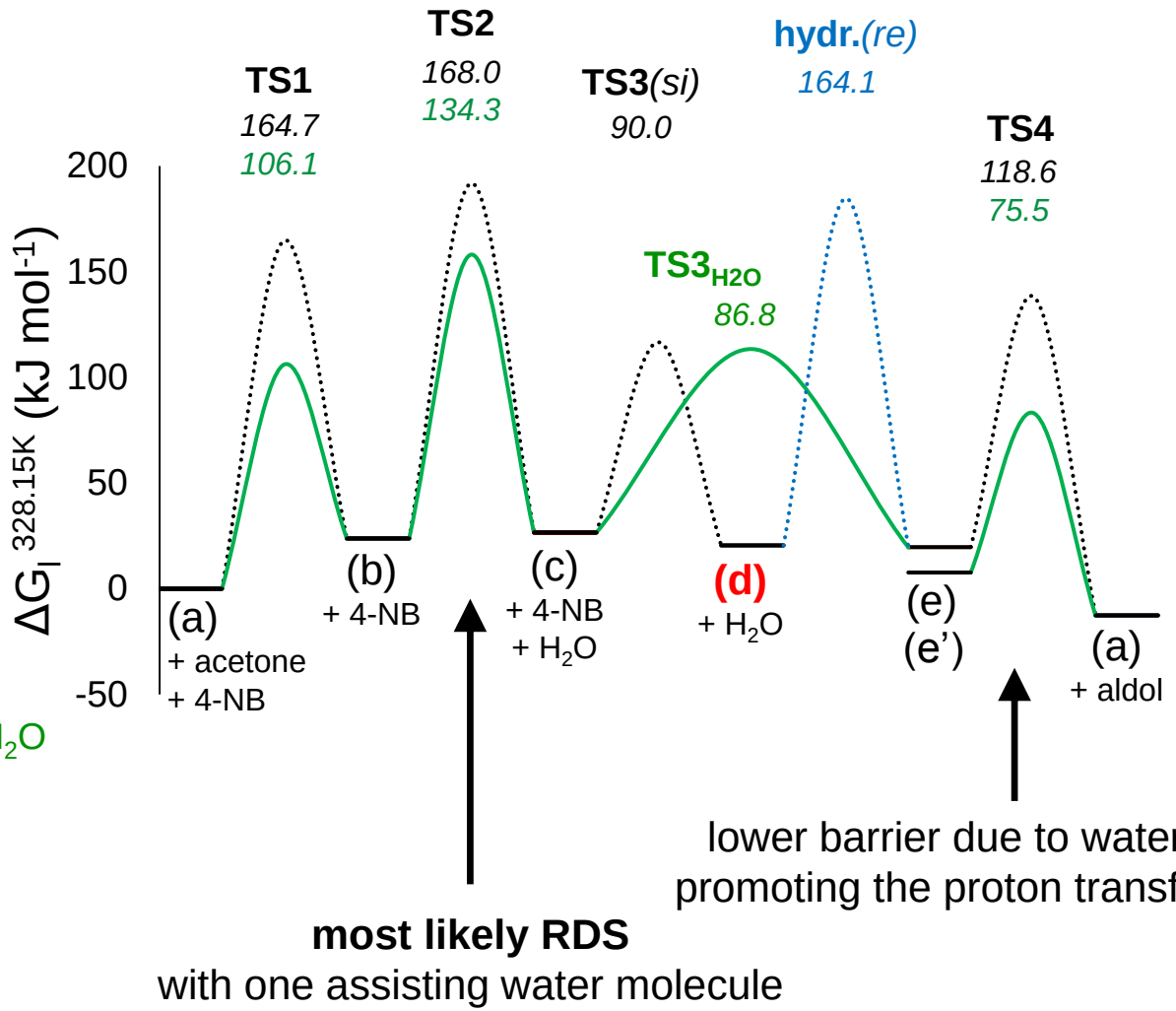
concerted addition-hydration bypasses intermediate **(d)**!

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water





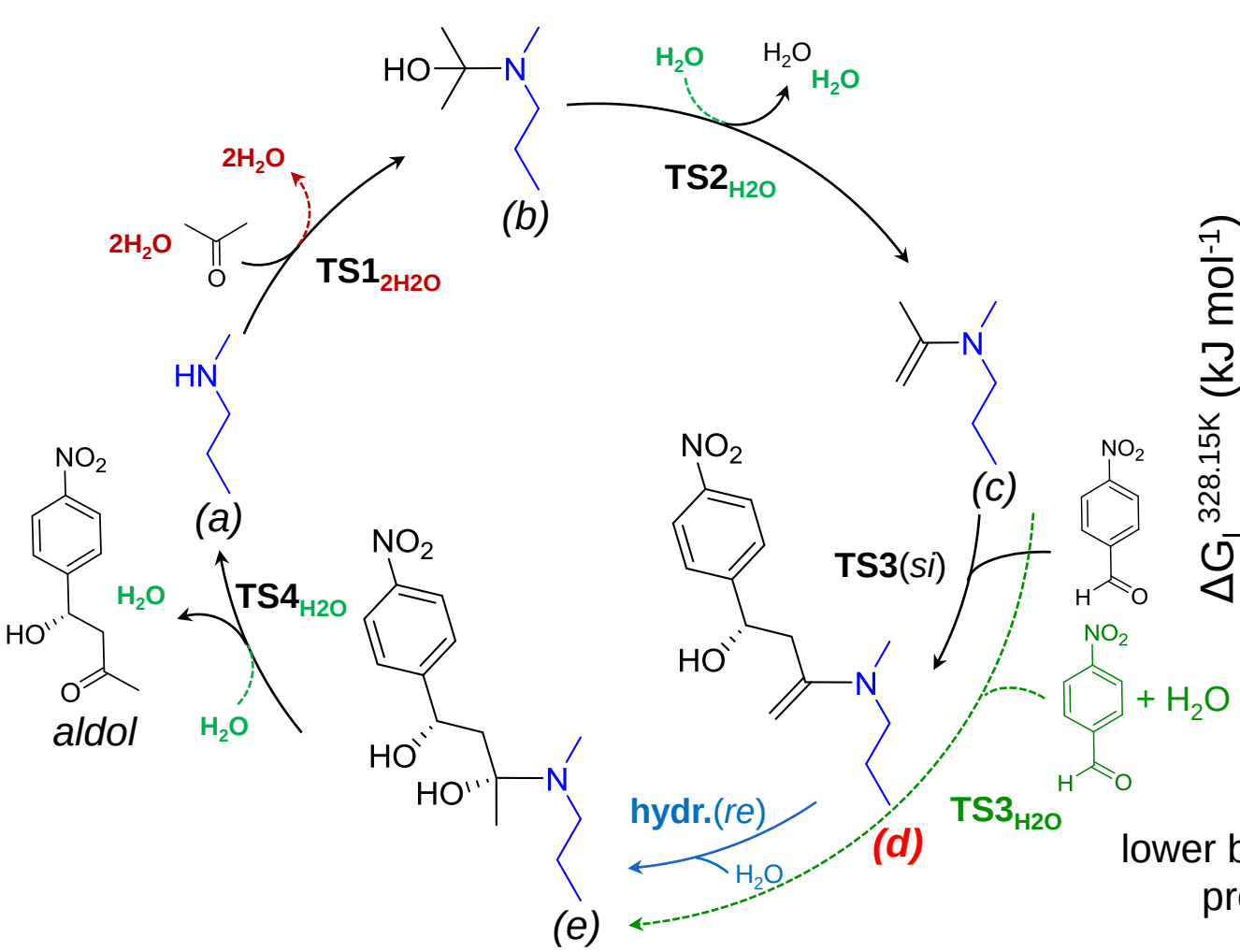
most likely RDS
with one assisting water molecule

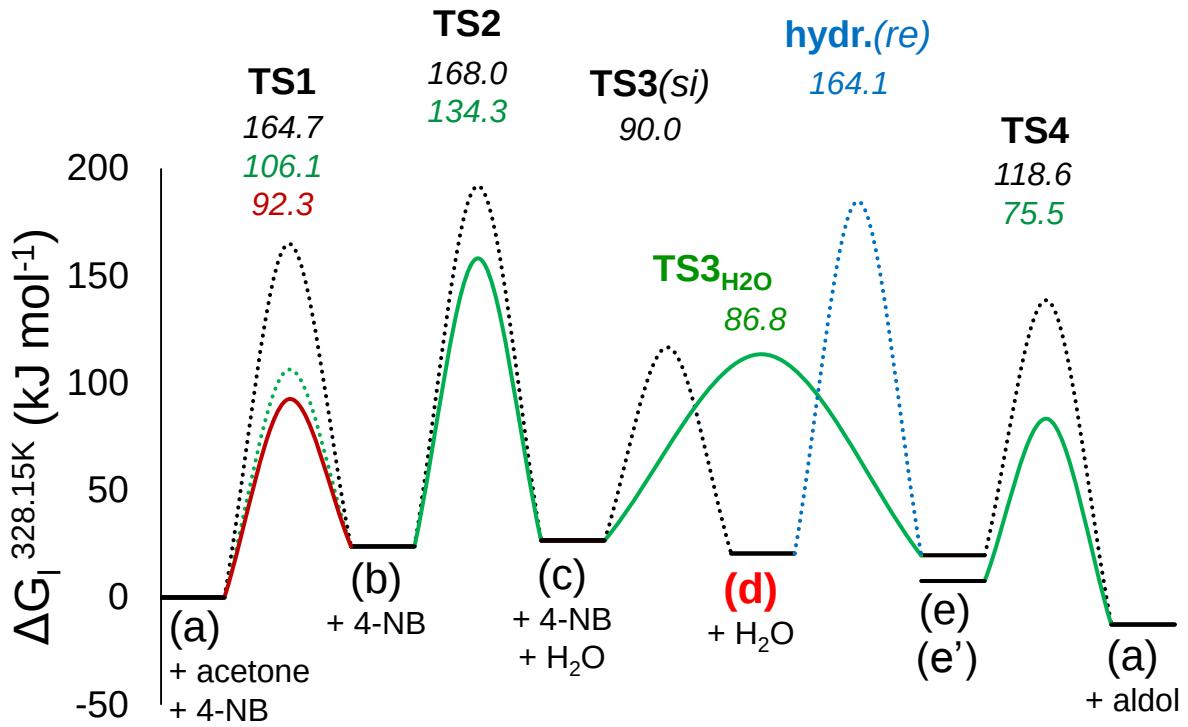
lower barrier due to water promoting the proton transfer

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water



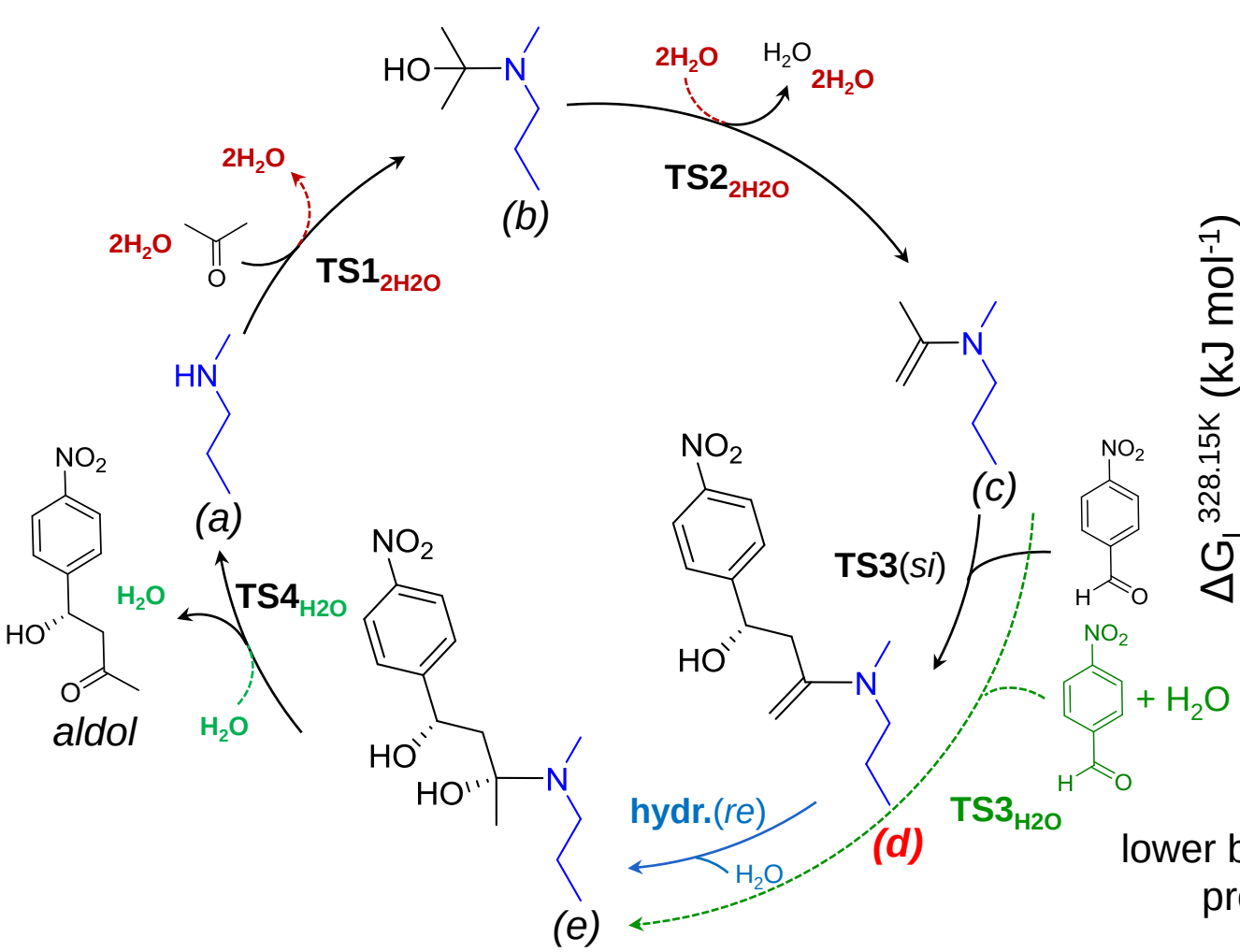


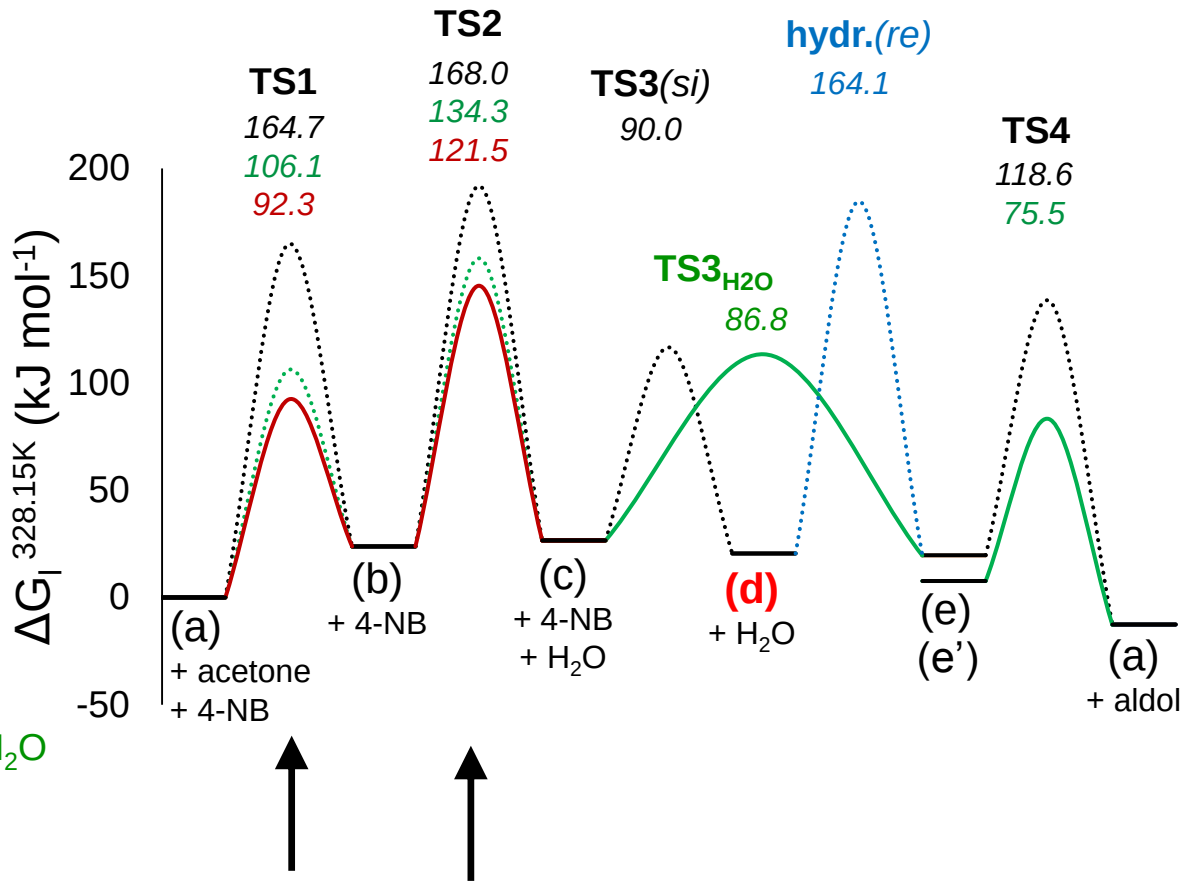
lower barrier due to 2 water molecules promoting the proton transfer

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water



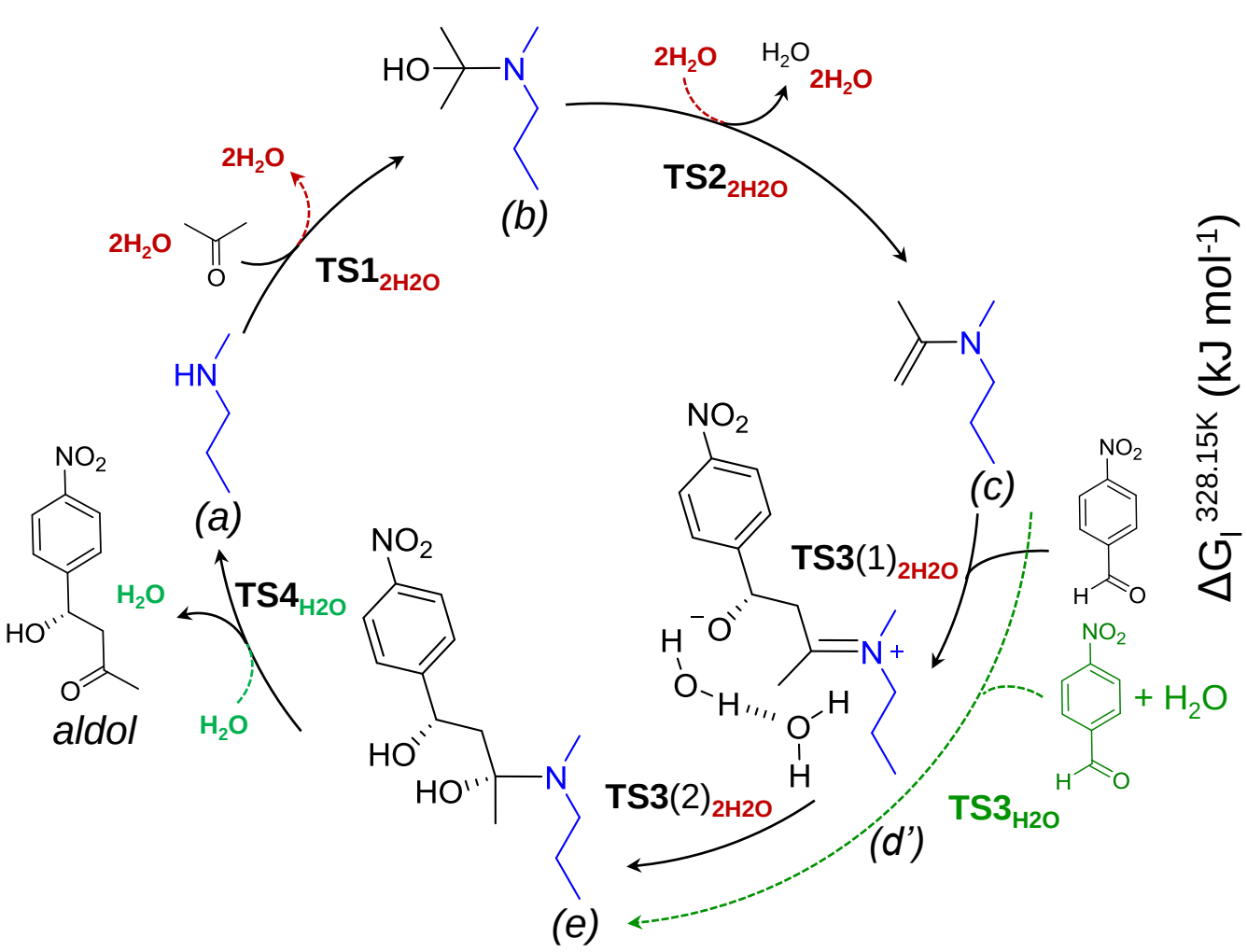


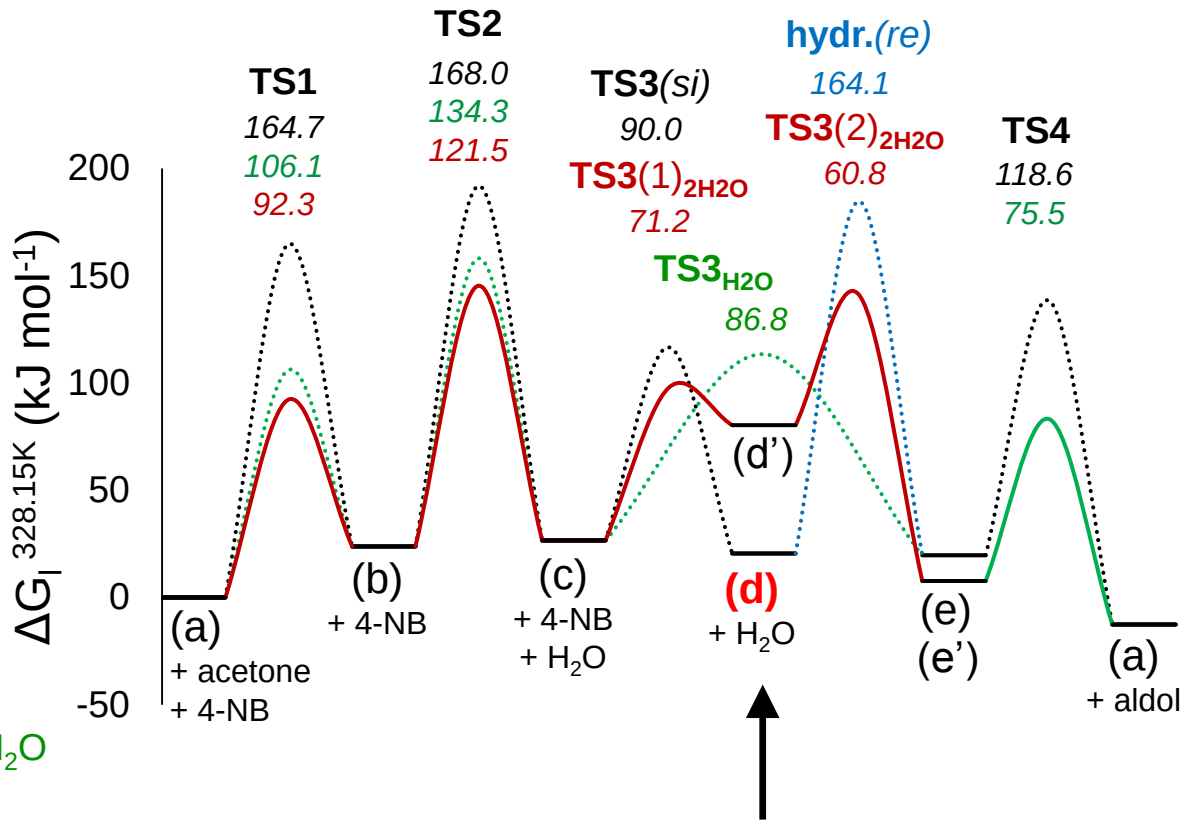
lower barrier due to 2 water molecules promoting the proton transfer

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water





iminium found as intermediate

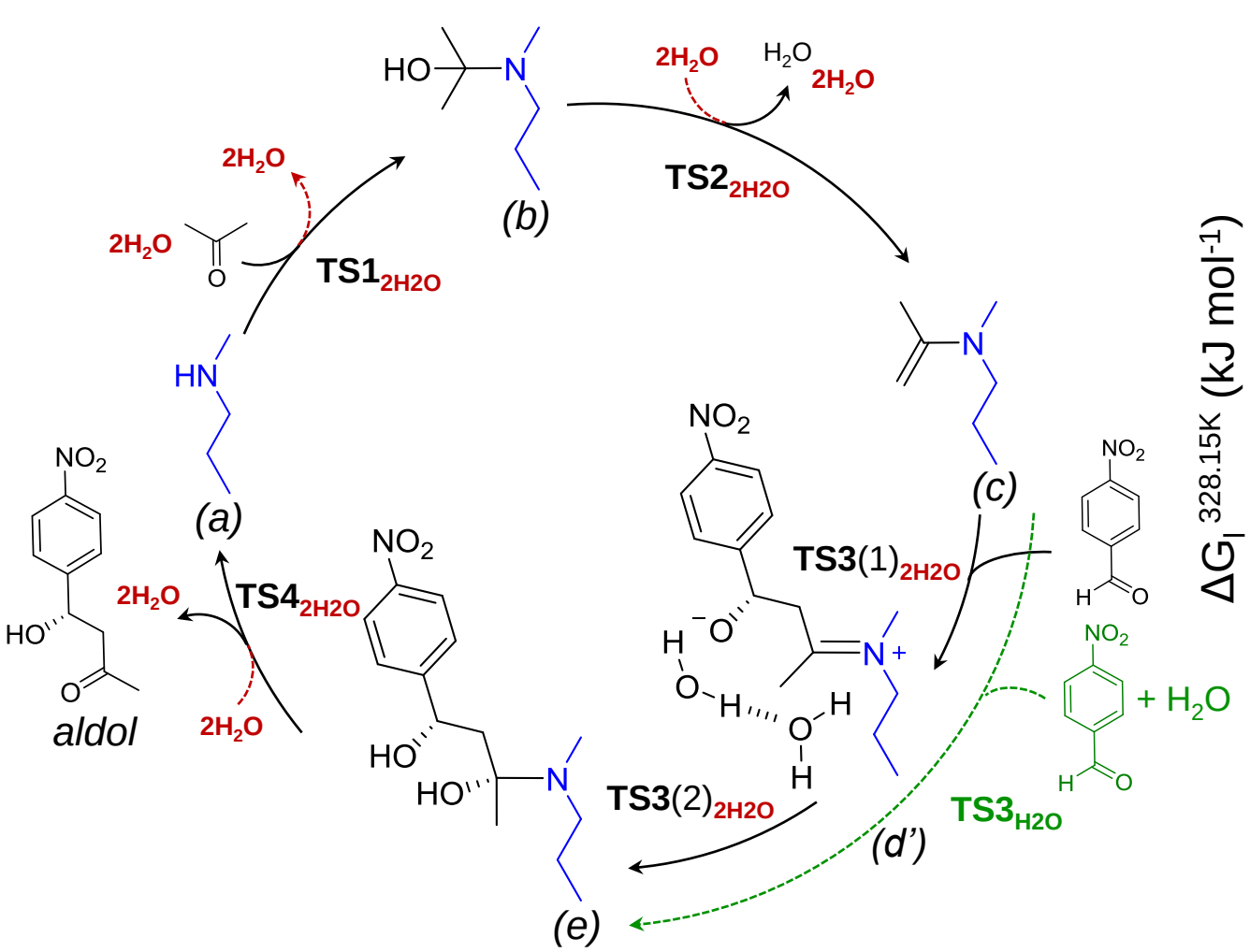
composite reaction barrier = **114.5 kJ mol^{-1}**

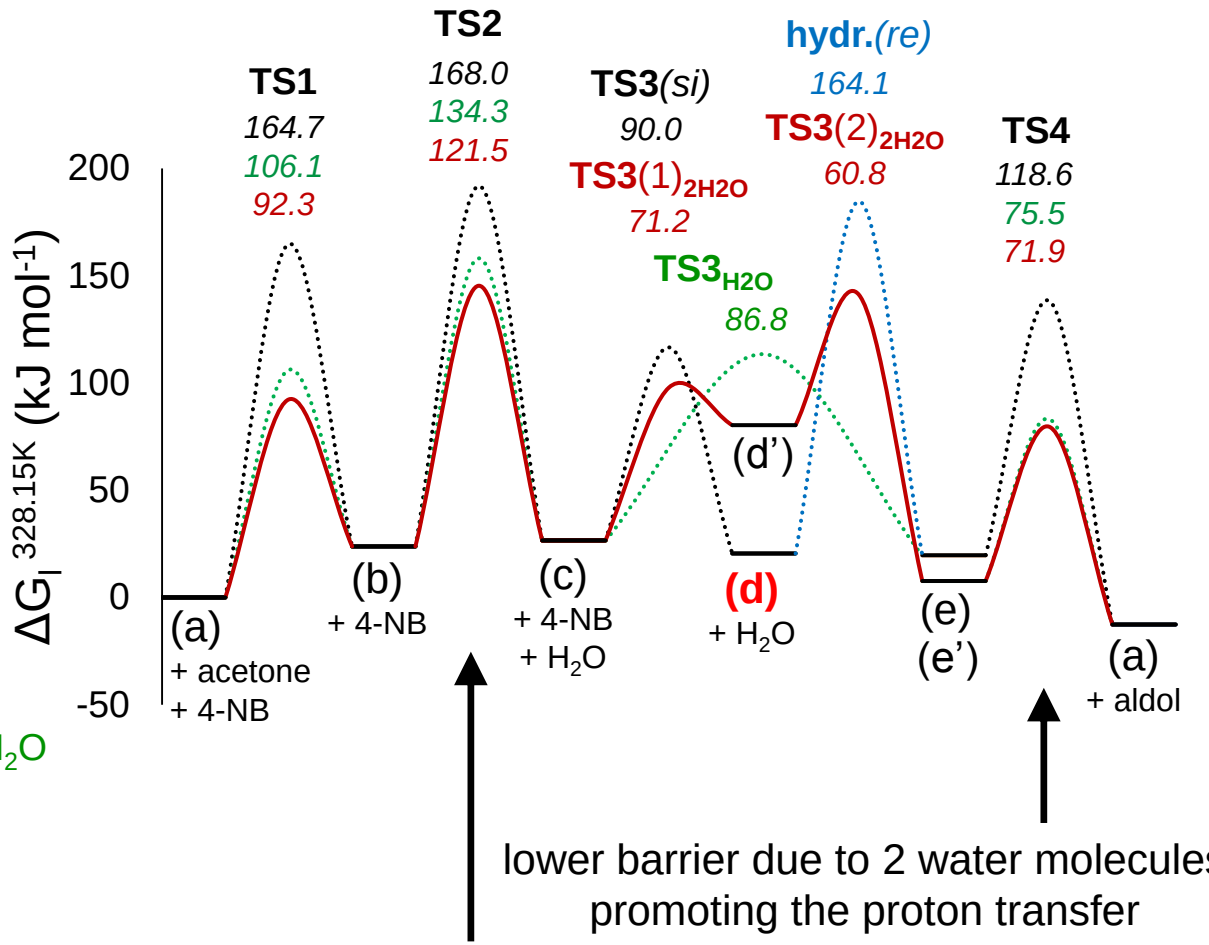
Higher than in the case of one assisting water molecule!

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water



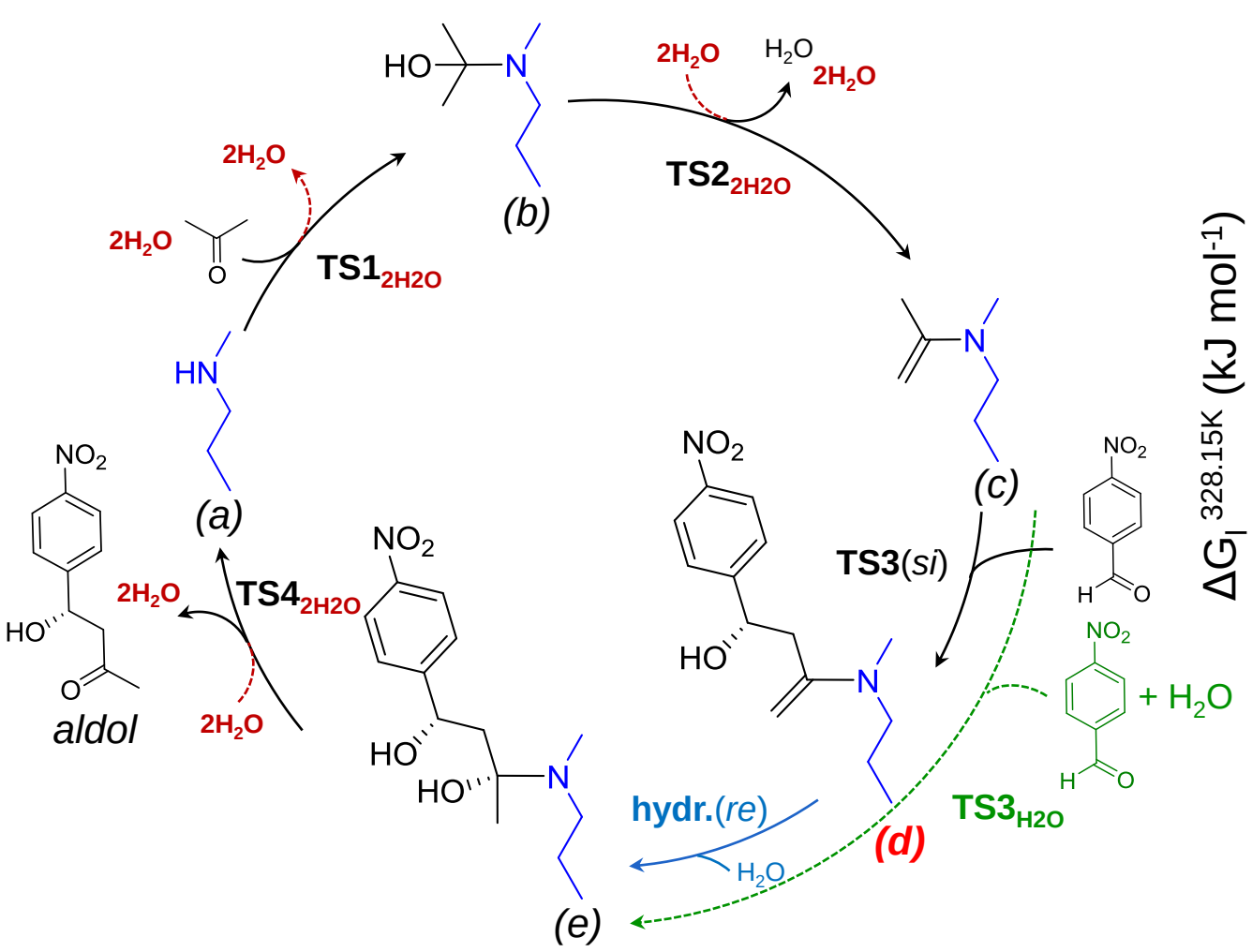


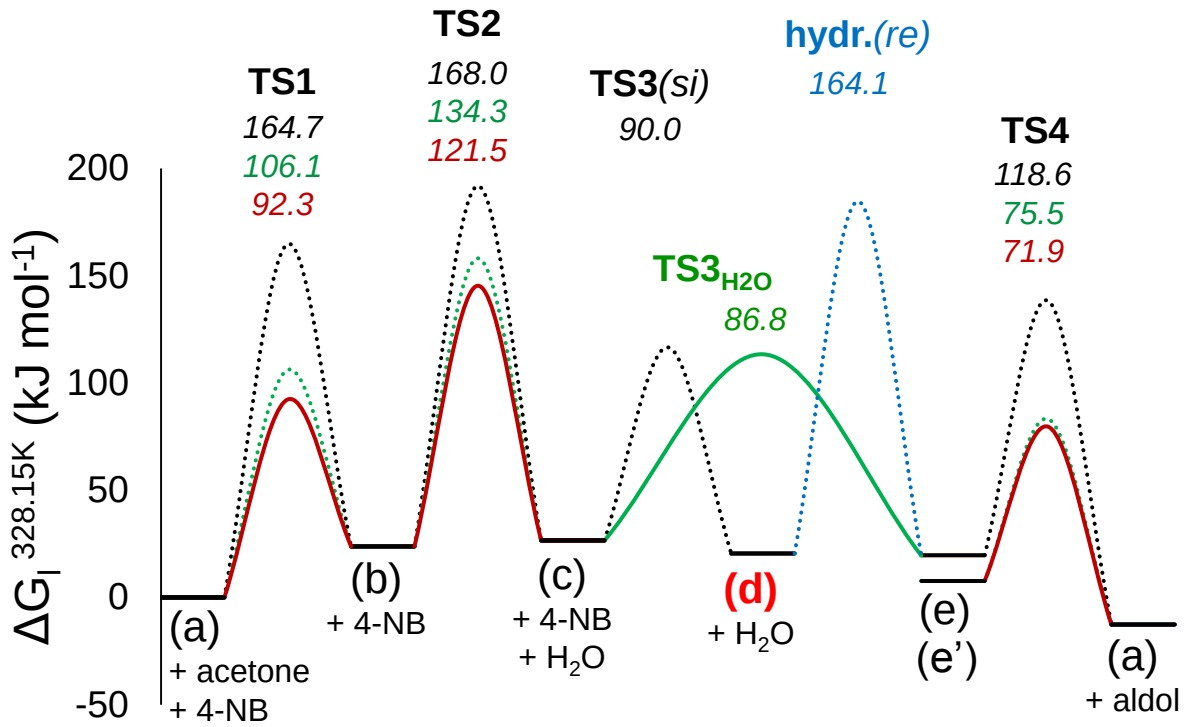
most likely RDS
with two assisting water molecules

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Aldol reaction mechanism: the effect of water





Change in bulk solvent polarity

50 vol% DMSO → **50 vol% hexane**

$TS1_{2H2O}$	$TS2_{2H2O}$	$TS3_{H2O}$	$TS4_{2H2O}$
78.9	***107.9***	***79.5***	***67.4***

- Effect of water is more pronounced!

$$\Delta G_{solv}(H_2O)_{hexane} > \Delta G_{solv}(H_2O)_{DMSO}$$

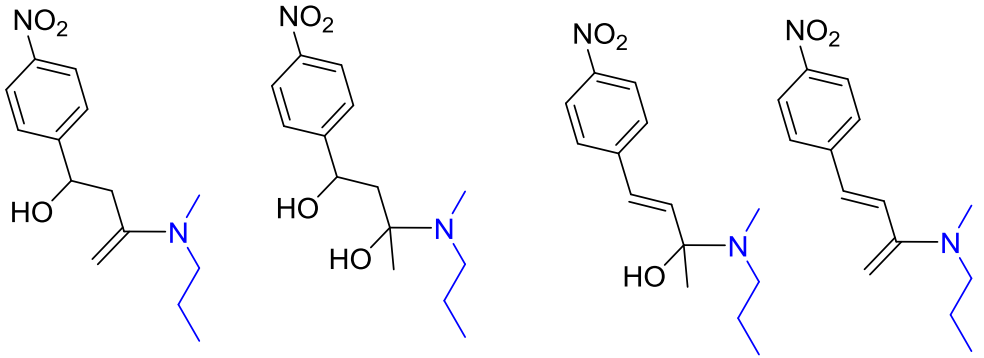
$$\gamma(H_2O)_{hexane} > \gamma(H_2O)_{DMSO}$$

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

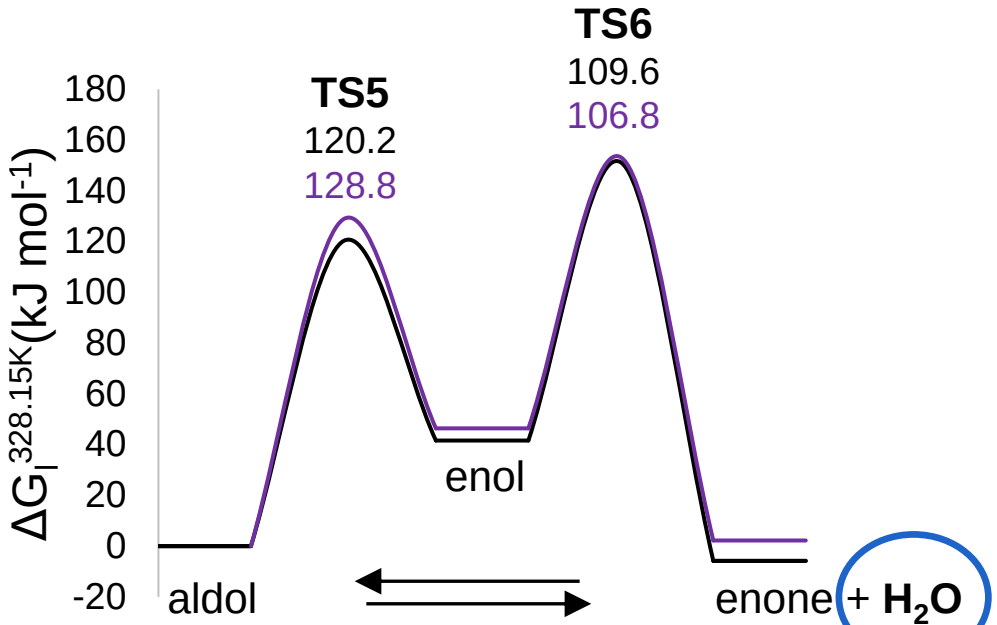
Site-blocking surface species

Experimentally identified in previous work[1]



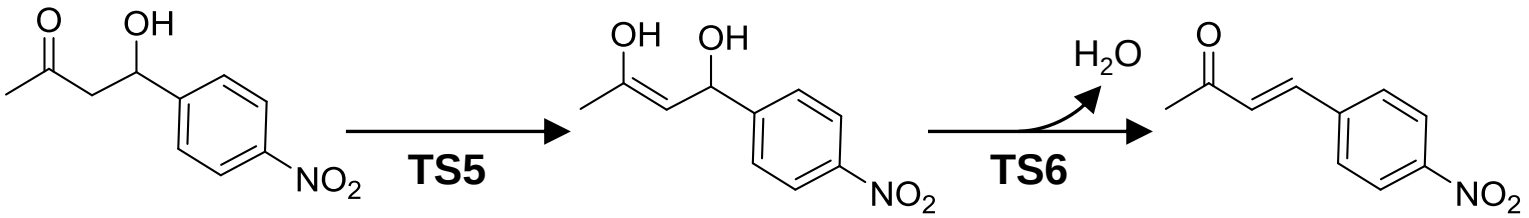
(d) *(e)* ***(f)*** ***(g)***

via enone product readsorption



$\Delta_r G_{DMSO}^{328K}$ = -5.82 kJ mol^{-1}

$\Delta_r G_{hexane}^{328K}$ = +2.22 kJ mol^{-1}



aldol enol enone

Shift equilibrium to the left by adding water!

1) De Vylder A, et al. J. Catal. 361. p.51-61 **2018**

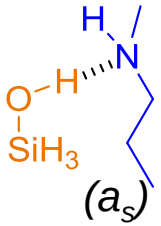
Outline

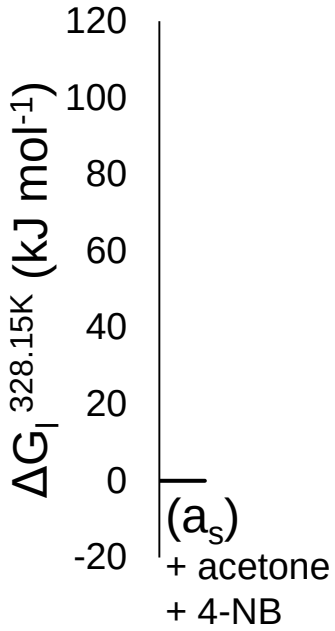
- Introduction
- The effect of water on site-blocking species in the amine catalyzed aldol reaction
- Silanol groups as promotor for the amine catalyzed aldol reaction
- Conclusions

GHENT UNIVERSITY

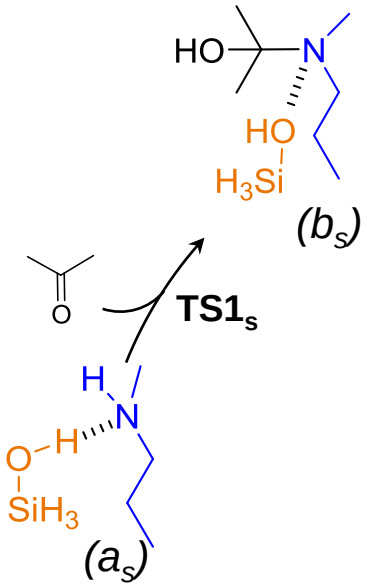
LCT DRIVING CHEMICAL TECHNOLOGY

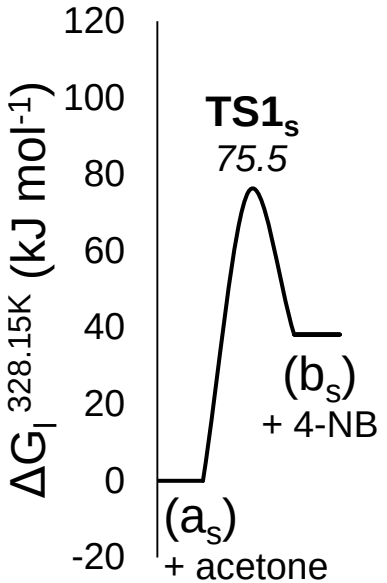
Promotion by **one isolated** silanol group





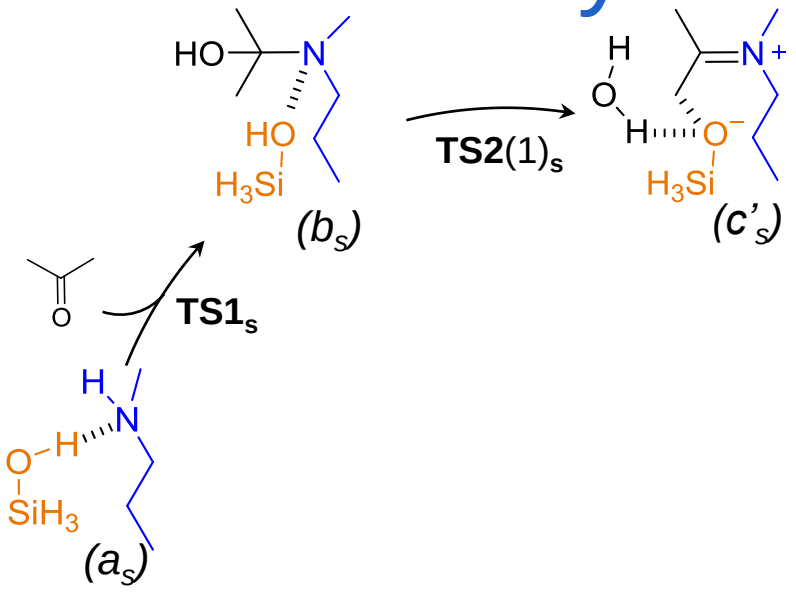
Promotion by **one isolated** silanol group

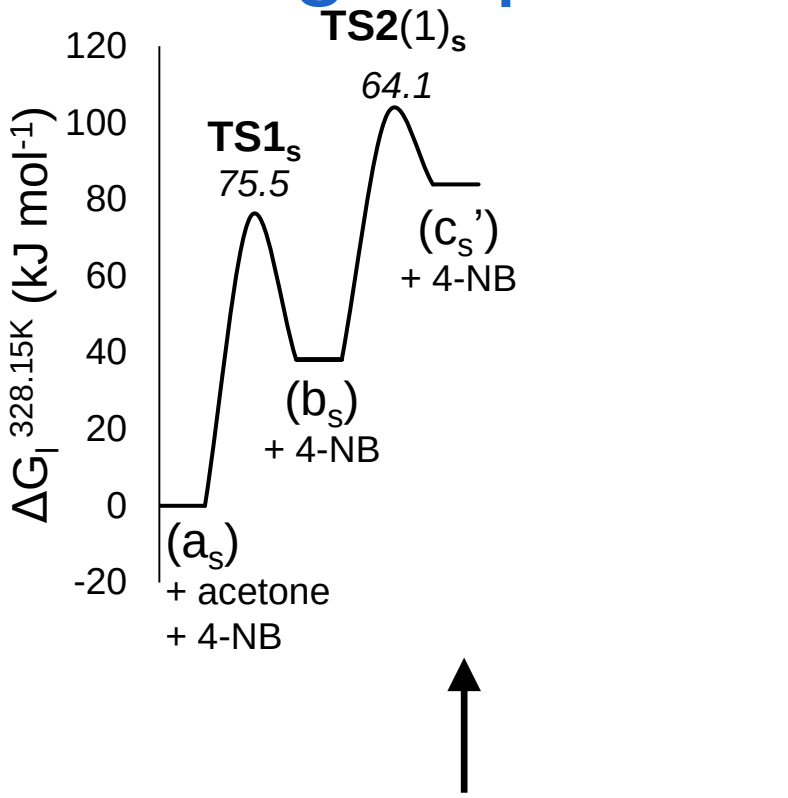




lower barrier than with water as proton transfer promotor

Promotion by **one isolated** silanol group



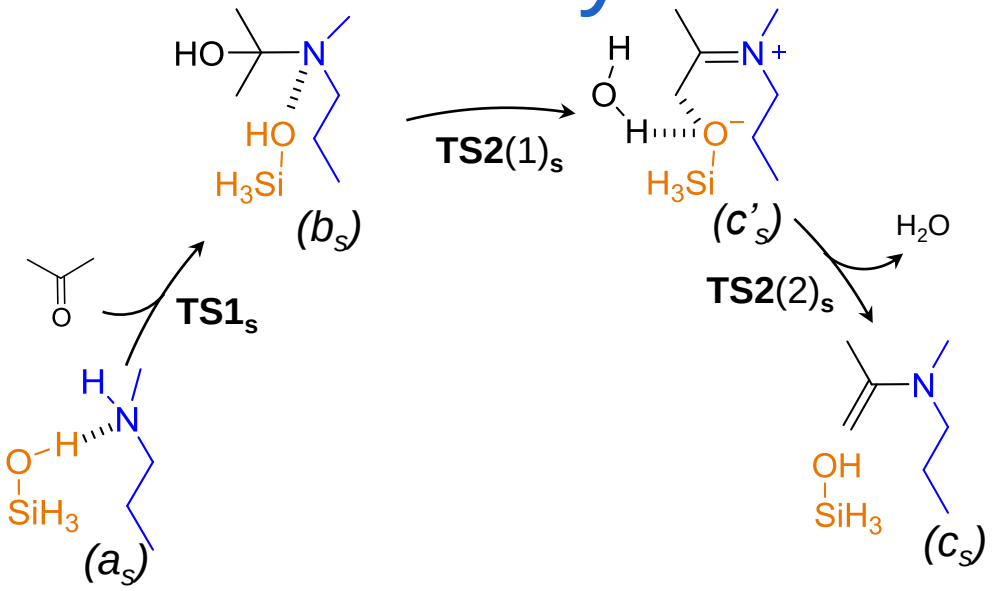


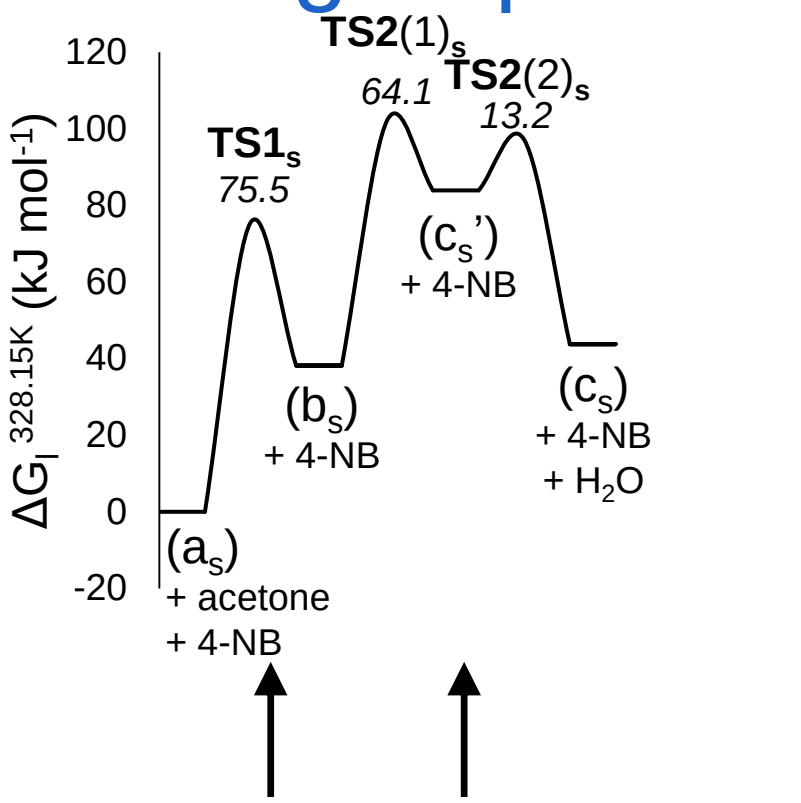
iminium ion found as intermediate

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Promotion by **one isolated** silanol group



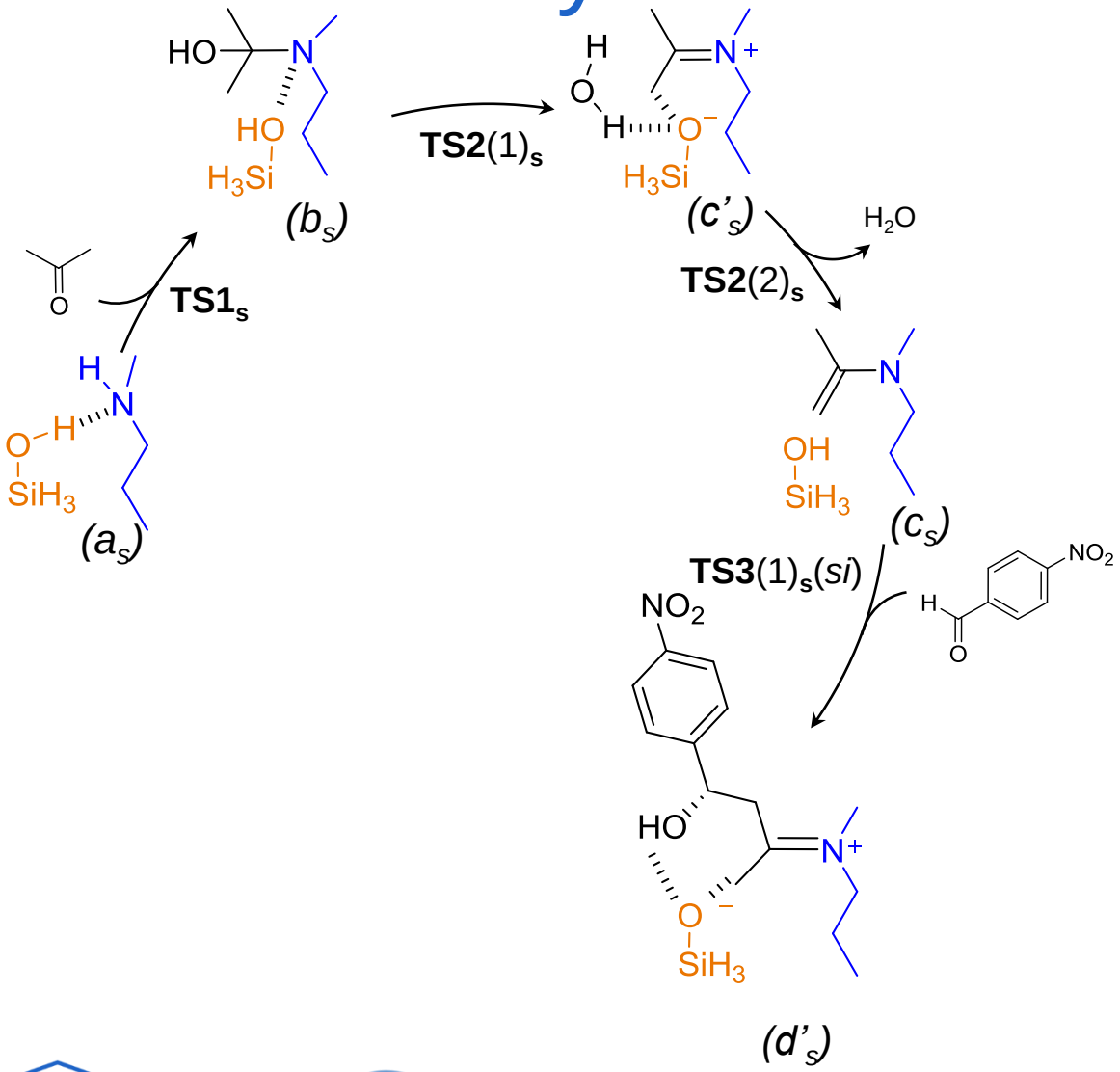


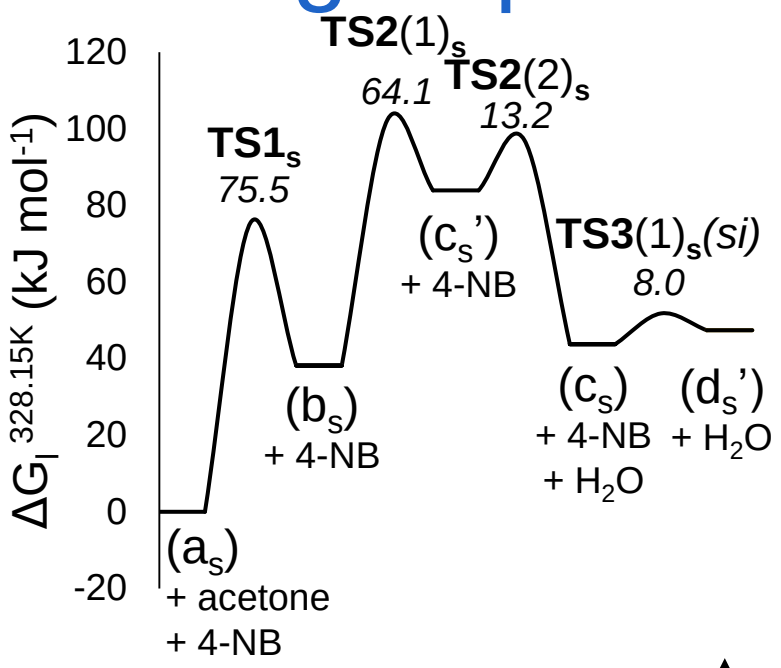
lower (composite) barrier than with water as proton transfer promotor

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Promotion by **one isolated** silanol group



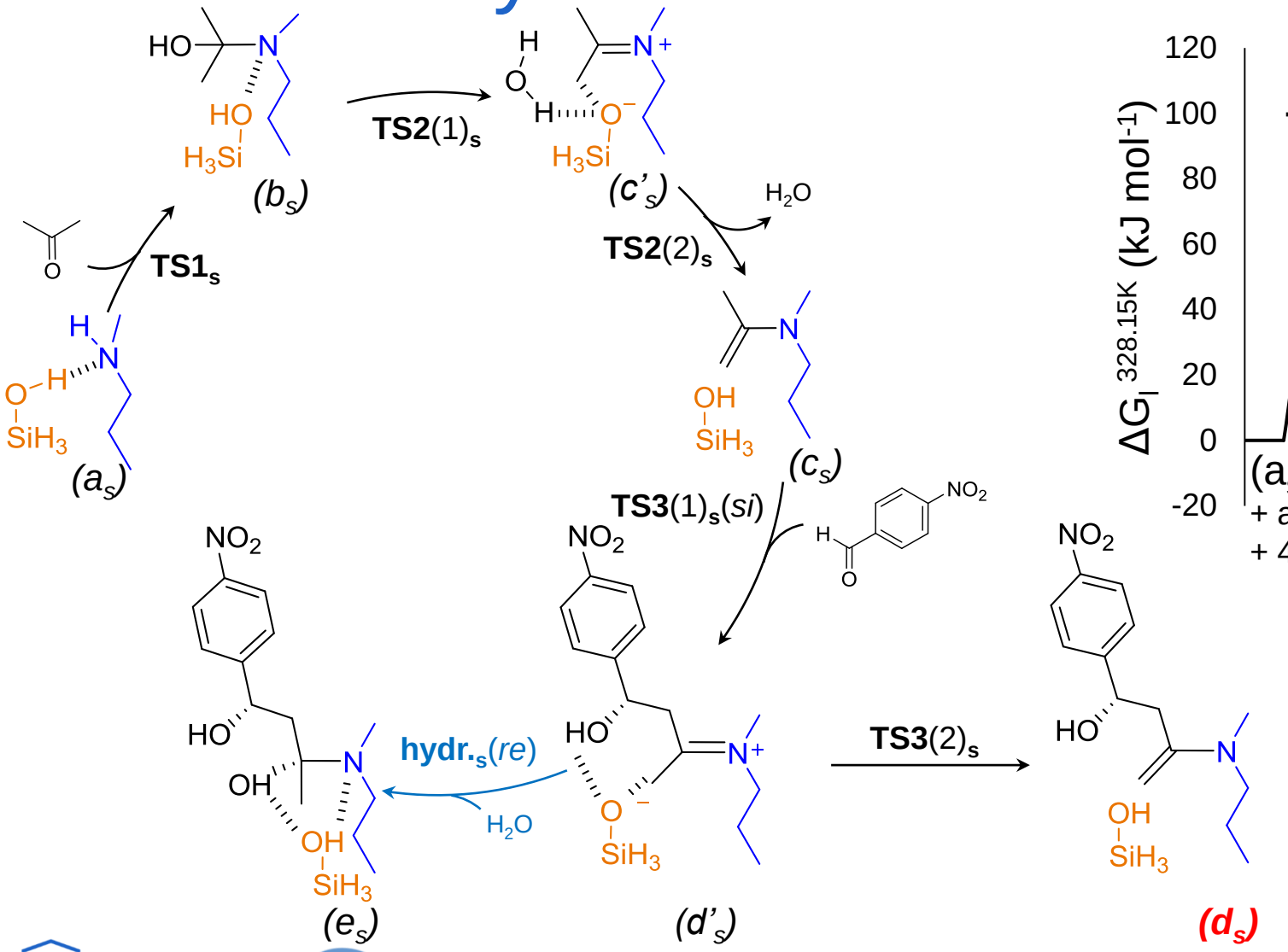


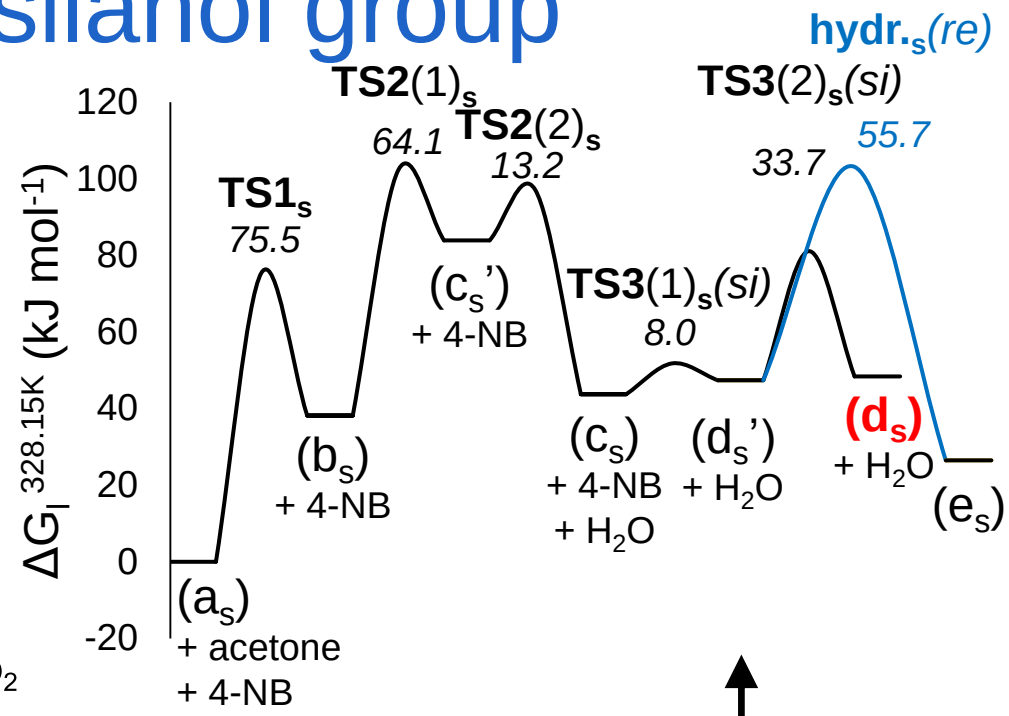
Iminium ion found as intermediate
Lower barrier than with water

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Promotion by **one isolated** silanol group





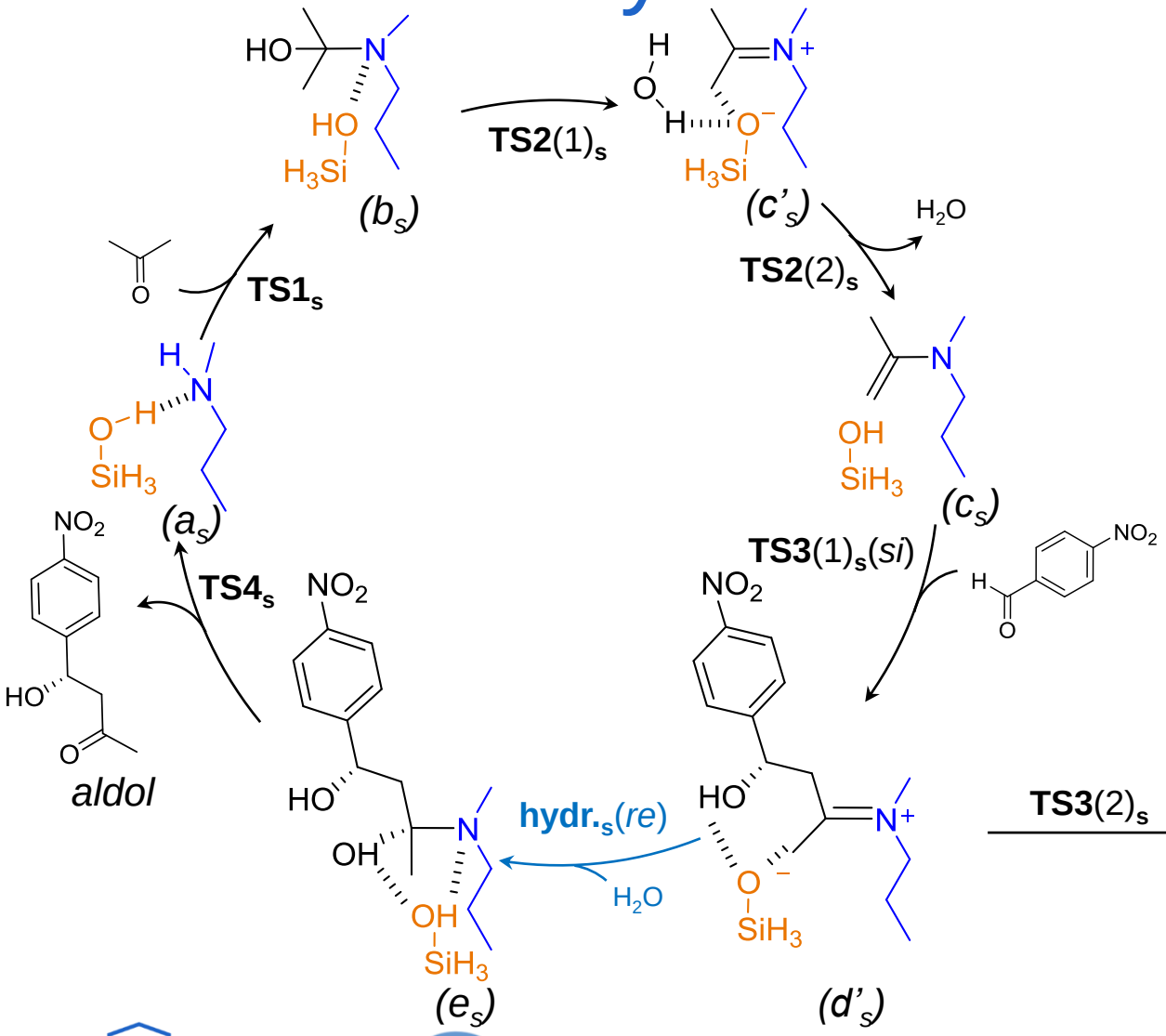
Proton transfer of the iminium intermediate with the silanol group yields intermediate **(d_s)**.

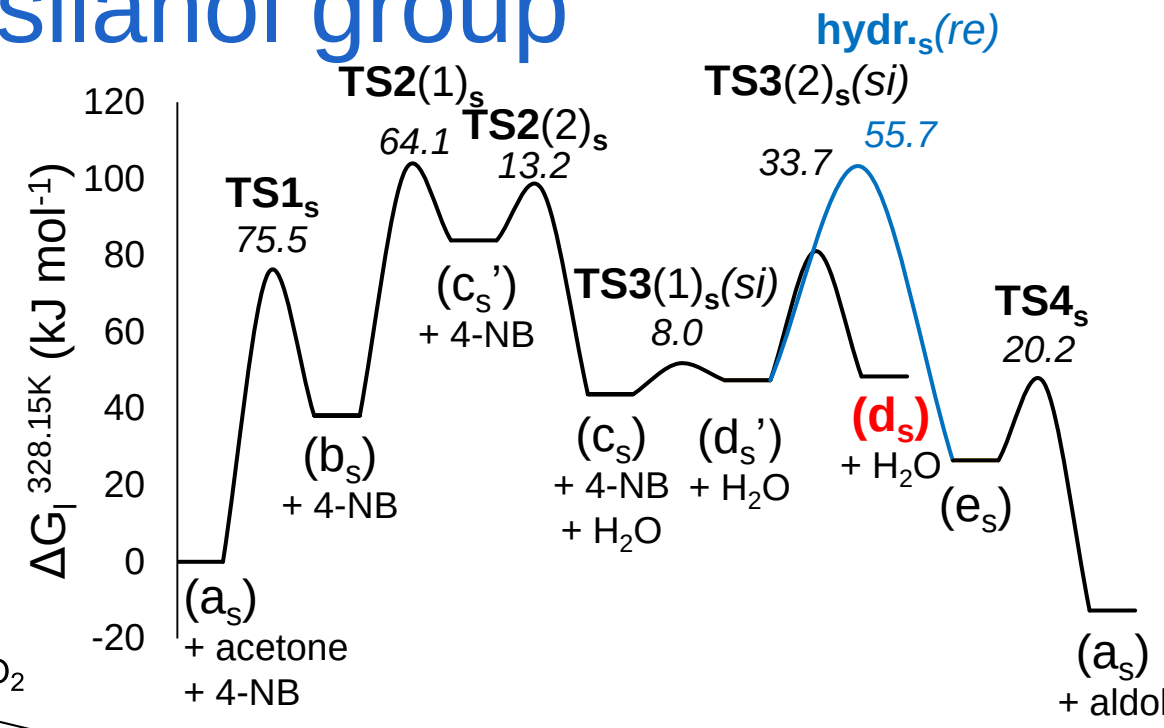
Hydration is the **most likely RDS** under dry reaction conditions

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Promotion by **one isolated** silanol group



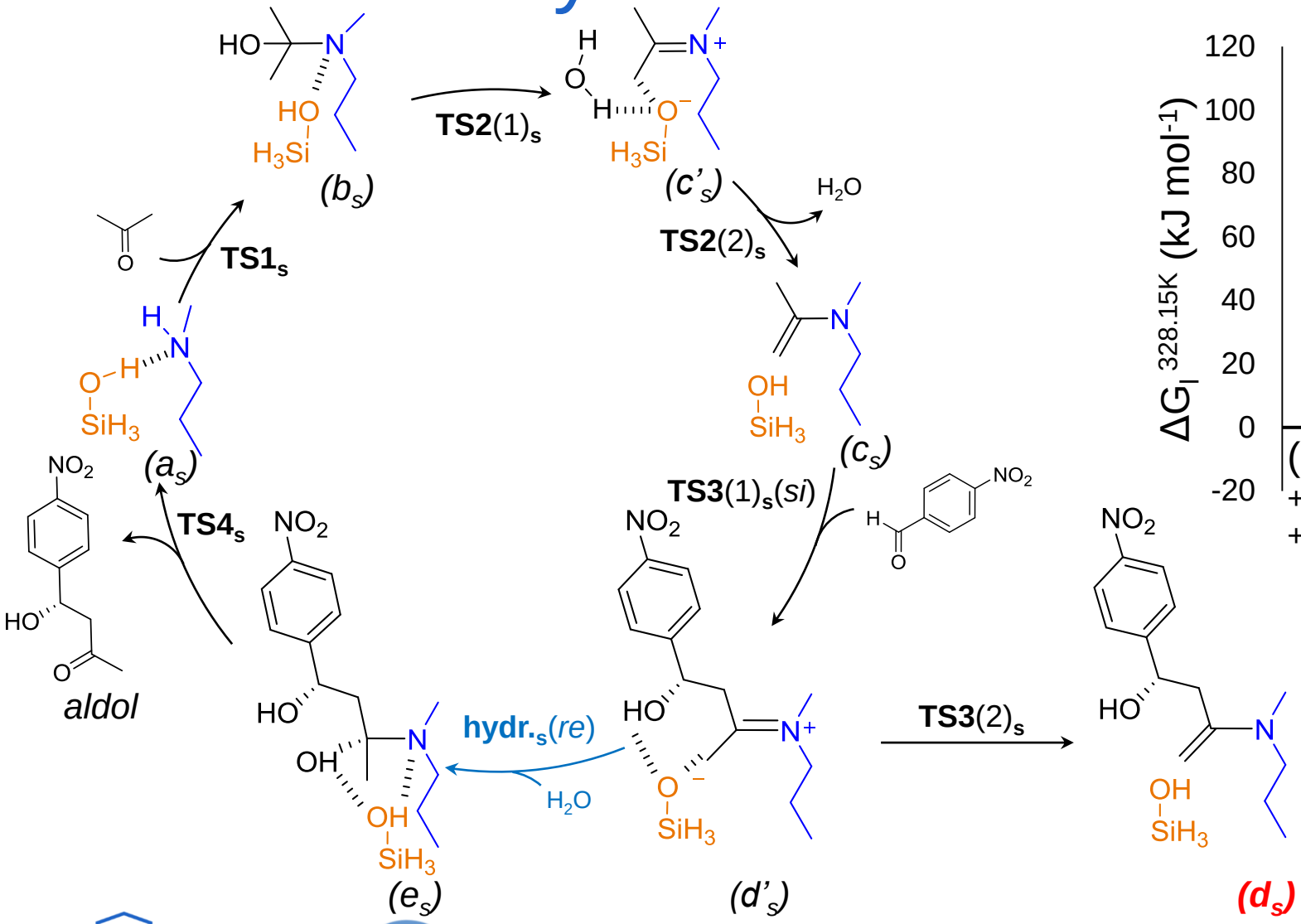


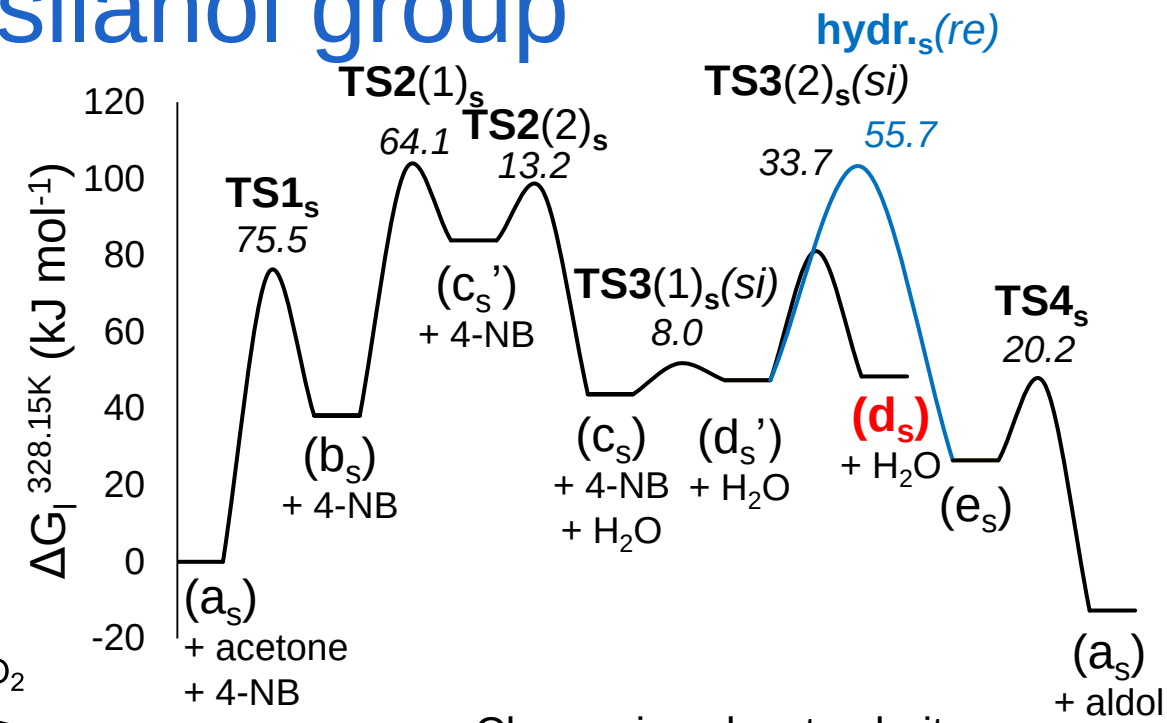
lower barrier than with water as proton transfer promotor

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Promotion by **one isolated** silanol group





Change in solvent polarity

50 vol% DMSO → **50 vol% hexane**

hydr.s(re)

46.1

- Effect of water is more pronounced!

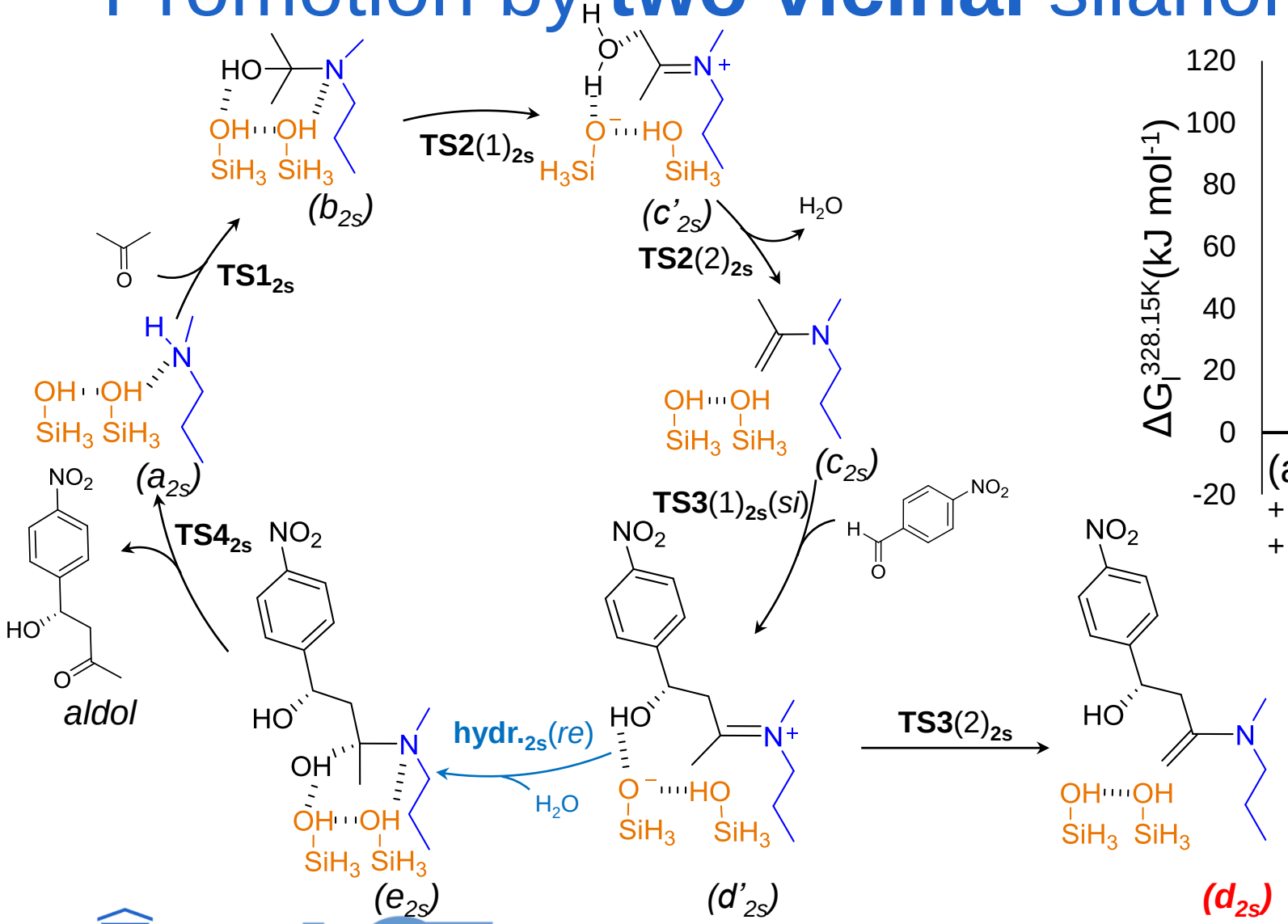
$\Delta G_{solv}(H_2O)_{hexane} > \Delta G_{solv}(H_2O)_{DMSO}$

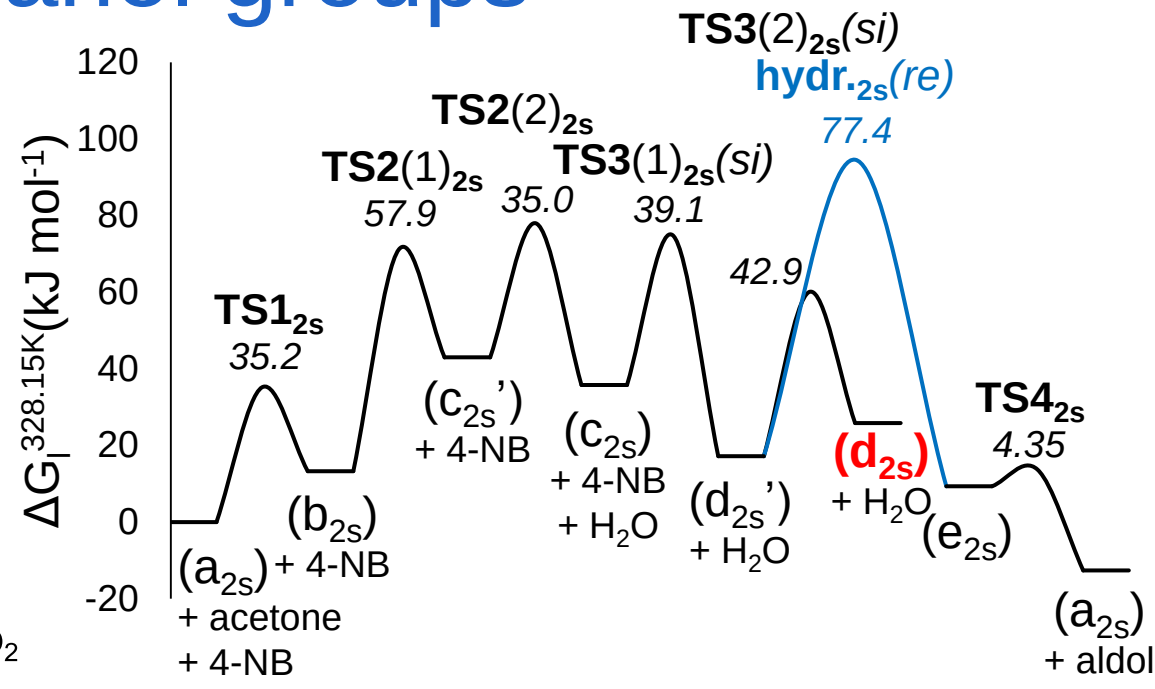
$\gamma(H_2O)_{hexane} > \gamma(H_2O)_{DMSO}$

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Promotion by **two vicinal** silanol groups





Iminium intermediates better stabilized with two vicinal silanols. This results in higher reaction barriers

Only adsorption/desorption barriers are lower than in the case of isolated silanol

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Outline

- Introduction
- The effect of water on site-blocking species in the amine catalyzed aldol reaction
- Silanol groups as promotor for the amine catalyzed aldol reaction
- Conclusions

GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

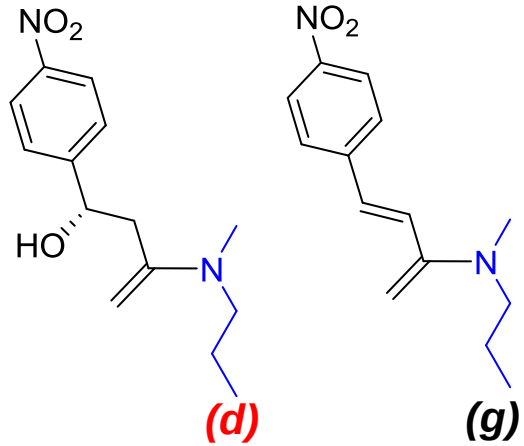
Conclusions

Water molecules promote **proton-transfers** in the aldol reaction mechanism

Silanols are better proton-transfer promotors than water

Successful modeling of the following **experimental observations**:

- Under **low water concentrations**
  - Species **(d)** is abundantly present on the catalyst surface
  - Enone product readsorption leads to species **(g)**
- Under **higher water concentrations**,
  - Formation of species **(d)** is reduced
  - Product selectivity is shifted away from the enone product



Due to a **higher thermodynamic activity of water**, the beneficial effect of water is more pronounced in **hexane** as compared to **DMSO**

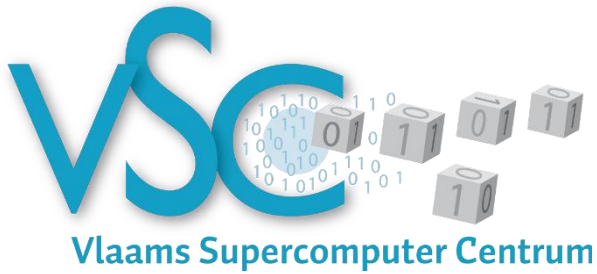
GHENT UNIVERSITY

LCT DRIVING CHEMICAL TECHNOLOGY

Acknowledgements

n° 615456

n° 3G006813
n° 12Z2218N



GHENT UNIVERSITY

LCT
DRIVING CHEMICAL TECHNOLOGY

LABORATORY FOR CHEMICAL TECHNOLOGY

Technologiepark 914, 9052 Ghent, Belgium

E info.lct@ugent.be
T 003293311757

https://www.lct.ugent.be

GHENT UNIVERSITY

LCT
DRIVING CHEMICAL TECHNOLOGY