COMPUTATIONAL CHEMISTRY DAY 2025

Experimental Work Guided by Computational Results: Reactions of Boronic Acids and Amines Give Structurally Diverse B←N Adducts

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How it all started...?

... Or how has a side reaction become the star?

Mechanochemistry (in our Laboratory)
– milling in a vibrational ball mill (mainly)
– PMMA jars that allow *in situ* Raman monitoring of the reaction

Suzuki-Miyaura reaction
– long-known and versatile cross coupling that affords a new C–C bond
– performed in the solid state since 2000

Pajić et al. *Chemistry-Methods*, **2025**, 30, e202400025

?

Organohalide (R–X, X = Br, I, sometimes Cl)
Boronic acid ($RB(OH)_2$)
Base (usually inorganic salt)
Palladium (pre)catalyst + ligand

$R–X + R'B(OH)_2 \longrightarrow R–R'$

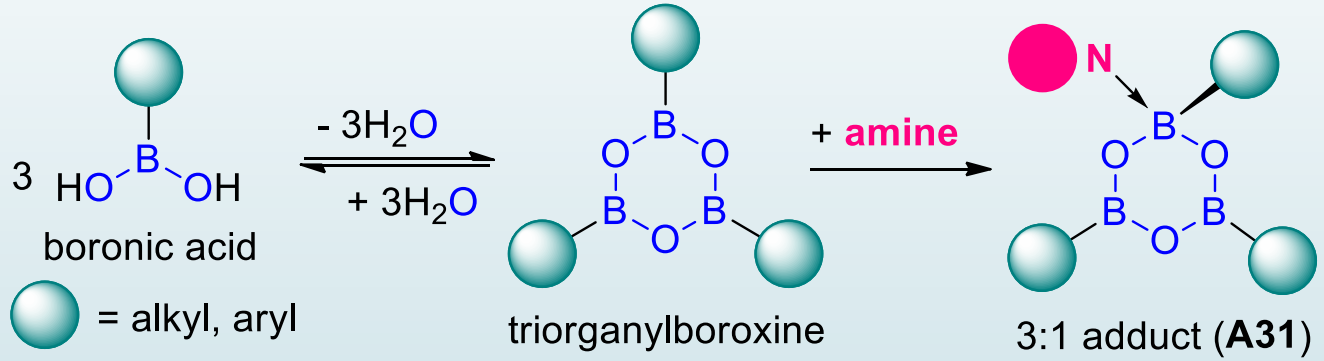
Additives?

Primary and secondary amines – fully inhibited reaction?!
(even though amines are used in solution to enhance the reaction)

Boronic acids and boroxines

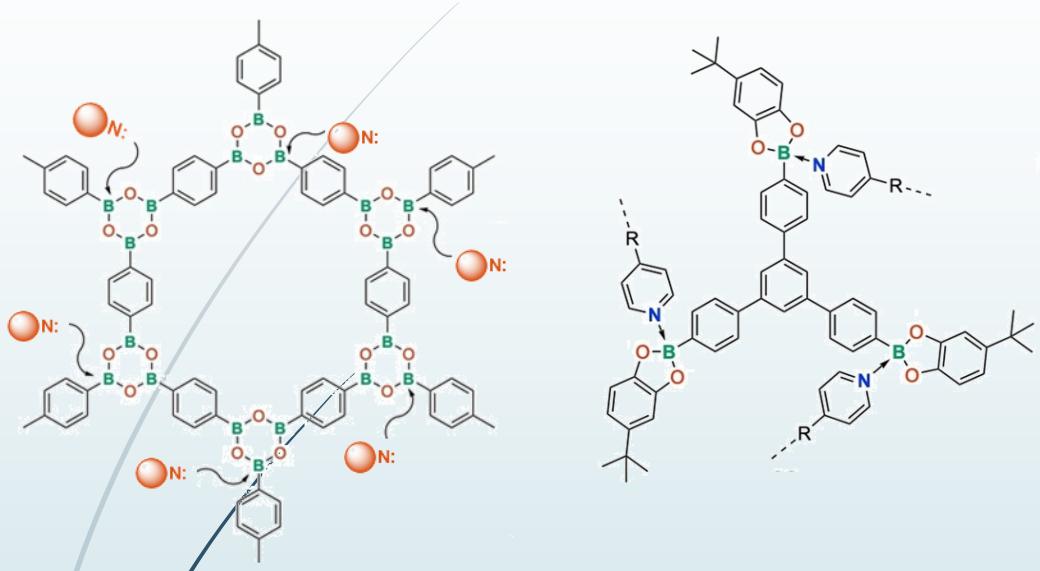
- cyclotrimeric anhydrides of boronic acids
- formed by a reversible entropically-favorable dehydration of boronic acids

Amine-facilitated trimerization of boronic acids:



- boron atoms in boroxines are Lewis acidic sites with a high affinity toward amines
- if amines are present, trimerization is amine-facilitated, quantitative and fast
- boronic acid first gives the corresponding boroxine, which reacts with the ligand (amine) usually forming one dative boron-nitrogen (B←N) bond

Boroxine-amine adducts

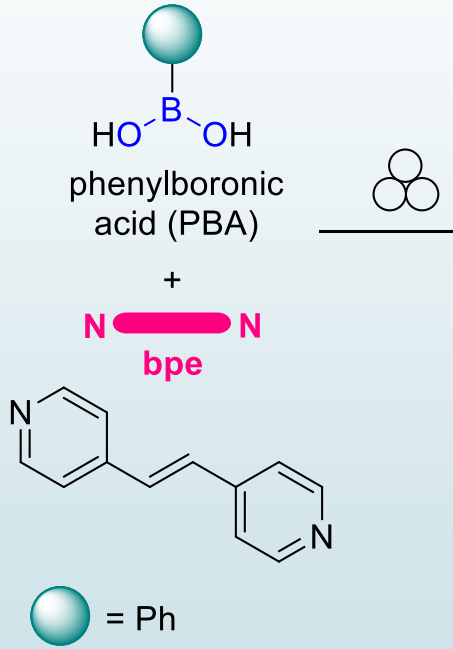


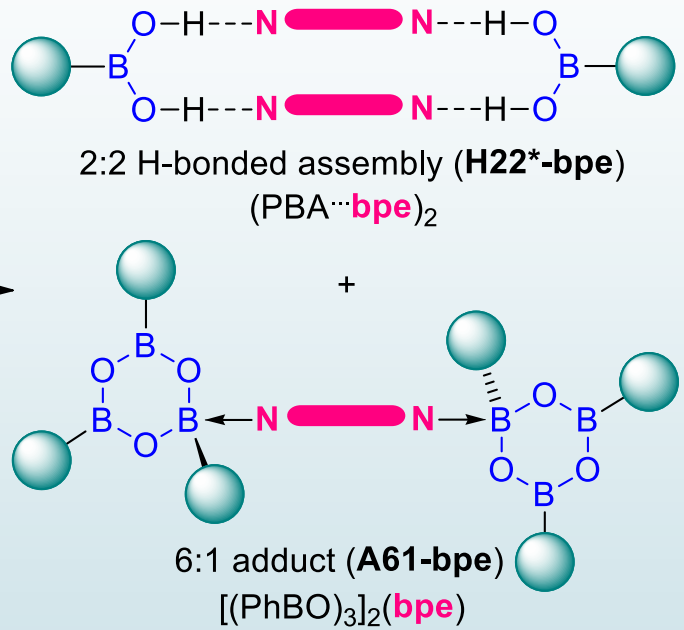
Structure: Molecular cages and sponges, 1D polymers, 3D networks, macrocycles…

Applications:
Optical and electronic materials
Host–guest complexes
Dynamic and self-healing polymers

Angew. Chem. Int. Ed. **2024**, 63, e202313379.

MacGillivray group (2023)



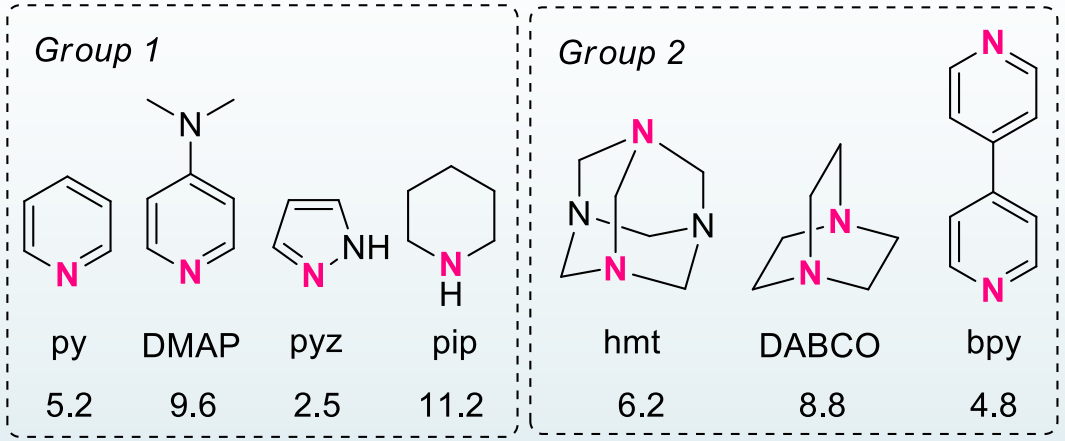


- **one amine**
- **coexistence** of B←N and H-bonds

Angew. Chem. Int. Ed. **2023**, 62, e202308350.

Structural diversity of B←N adducts

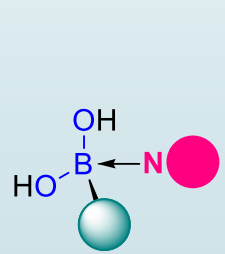
Selected amines:



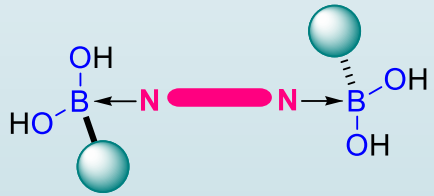
Solid or liquid?
Bonding site: 1 or 2 (more?)
Aliphatic or aromatic?
Range of pK_a values

N = any amine
N—N = Group 2 amine
= Ph

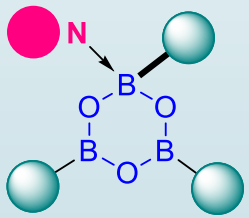
Plethora of plausible B←N adducts:



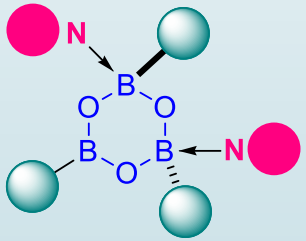
1:1 adduct (**A11**)
(PBA)(**amine**)



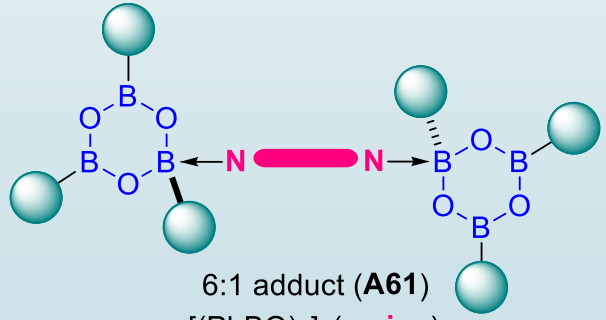
2:1 adduct (**A21**)
$(PBA)_2$(**amine**)



3:1 adduct (**A31**)
$(PhBO)_3$(**amine**)



3:2 adduct (**A32**)
$(PhBO)_3{\cdot}(\text{amine})_2$



6:1 adduct (**A61**)
$[(PhBO)_3]_2$(**amine**)

Even more possible structurally similar H-bonded structures.

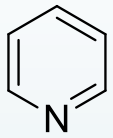
Calculations?

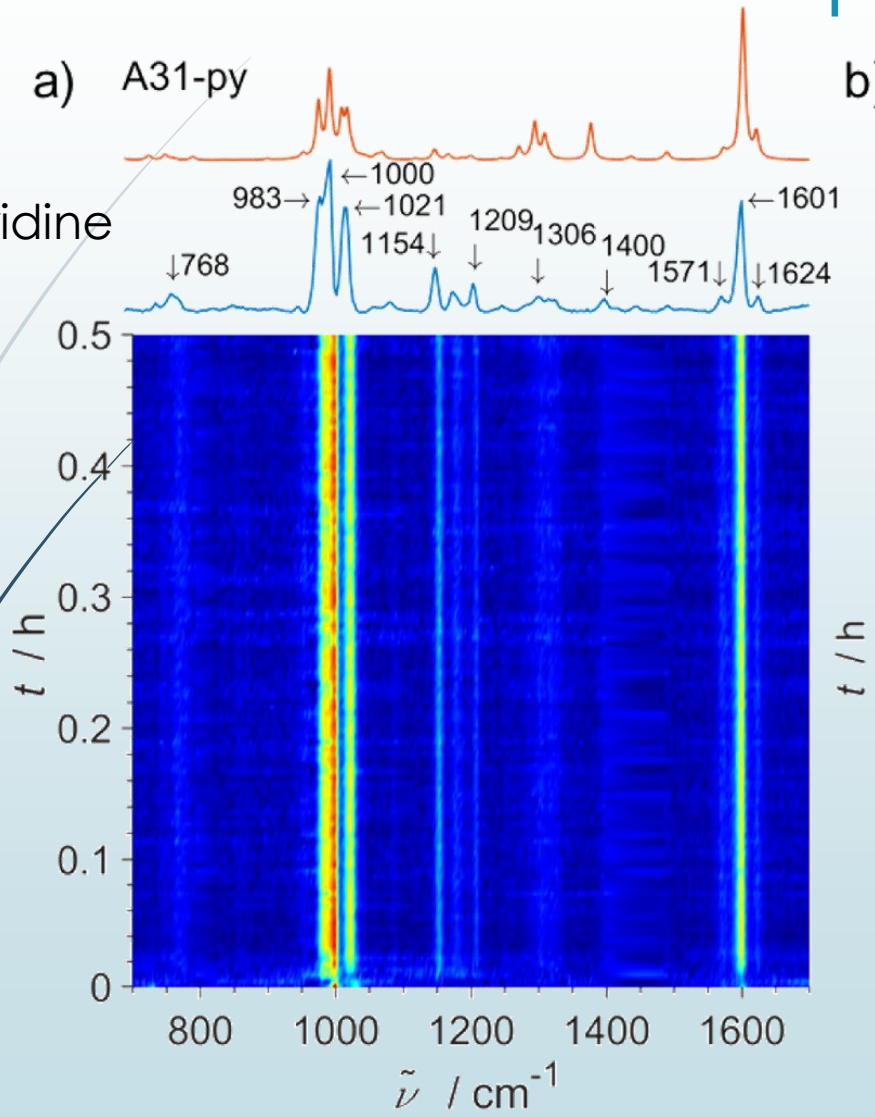
Gaussian16-C.01: b3lyp-gd3bj/def2tzvp
gas phase, IEF-PCM for chloroform and acetone

py / pip

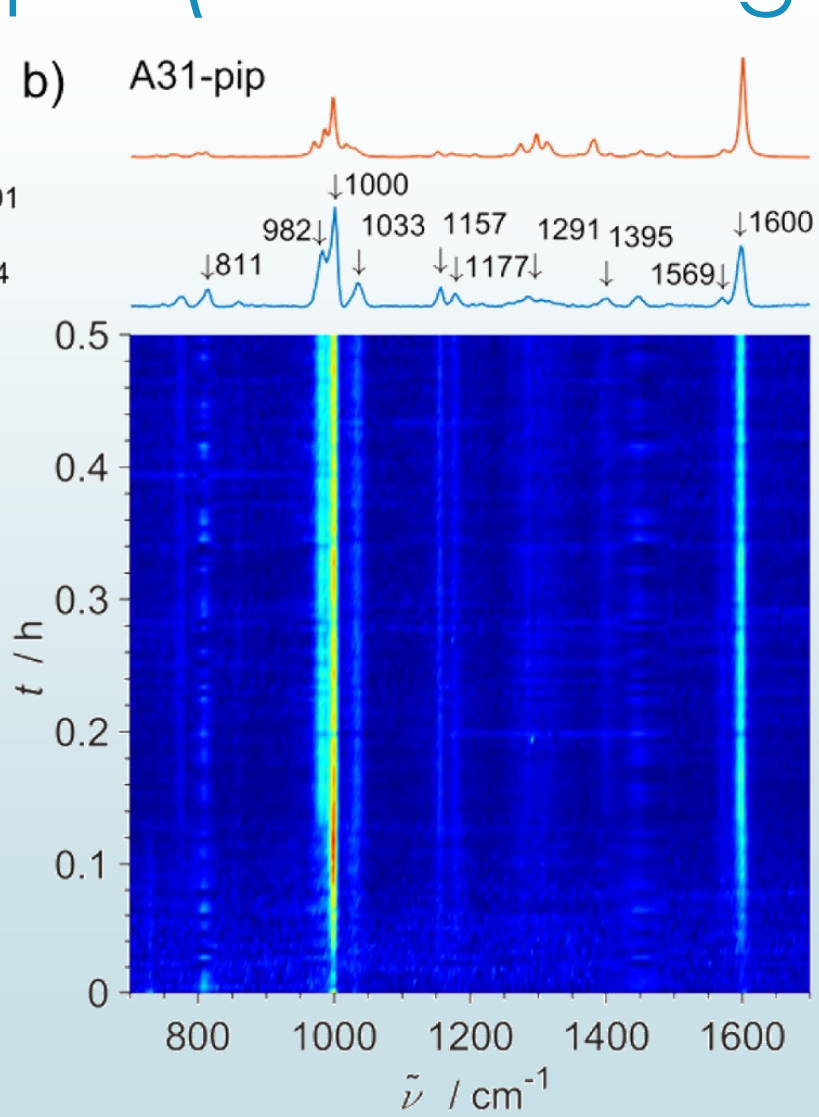
Let's start simple (with smelling liquids)

pyridine





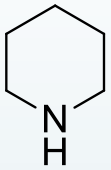
NG (**PBA** : **py** = 3 : 1)

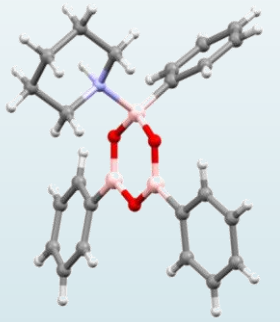


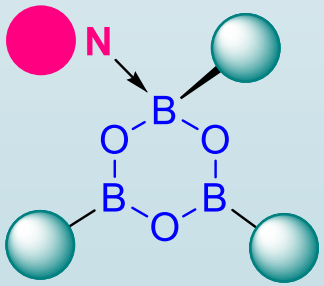
NG (**PBA** : **pip** = 3 : 1)

Fast and quantitative!

piperidine

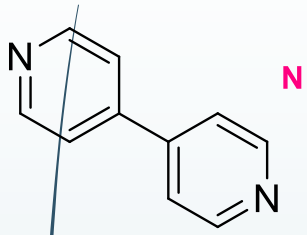


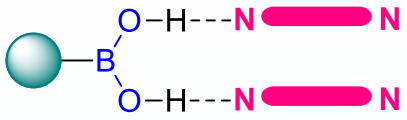




3:1 adduct (**A31**)
$(PhBO)_3$·(**amine**)

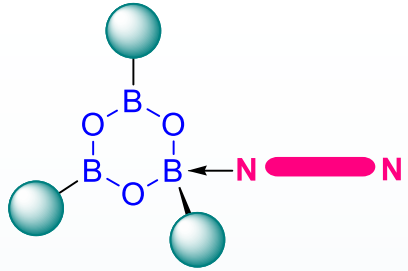
bpy



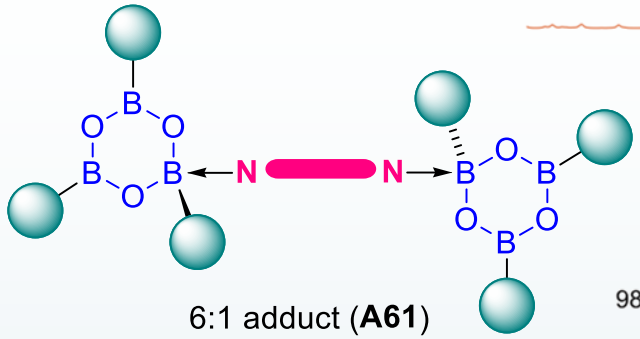


1:2 H-bonded assembly (**H12**)

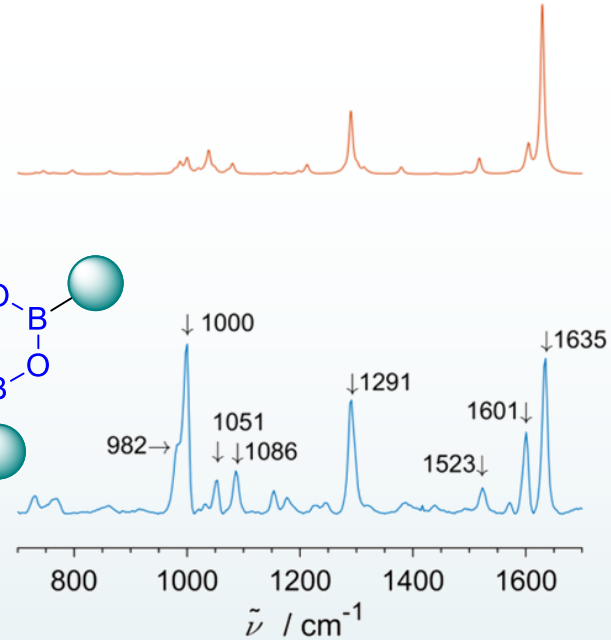
N N = amine = Ph

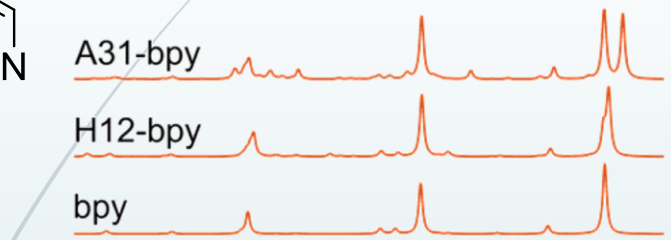


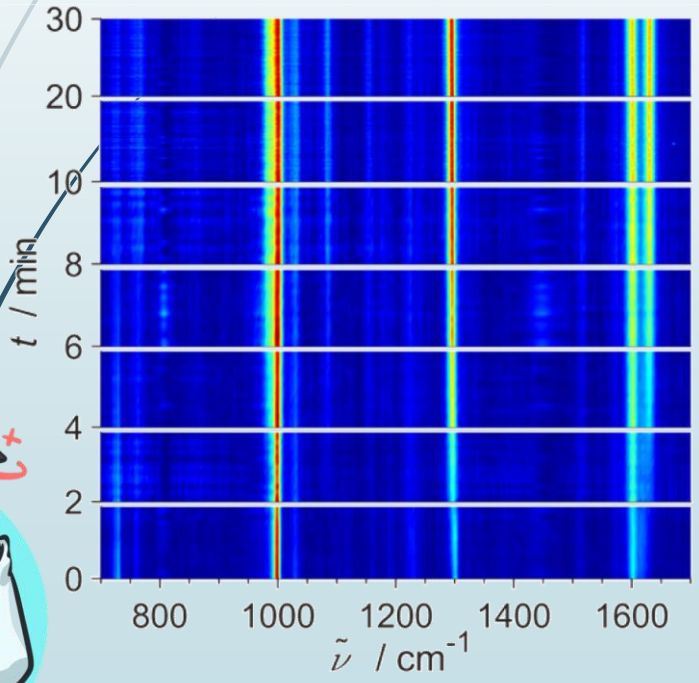
3:1 adduct (**A31**)



6:1 adduct (**A61**)

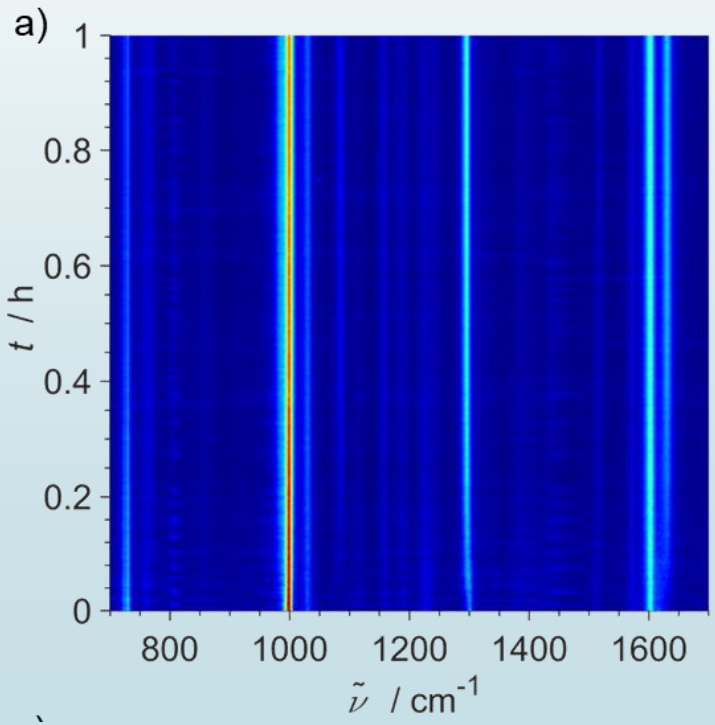




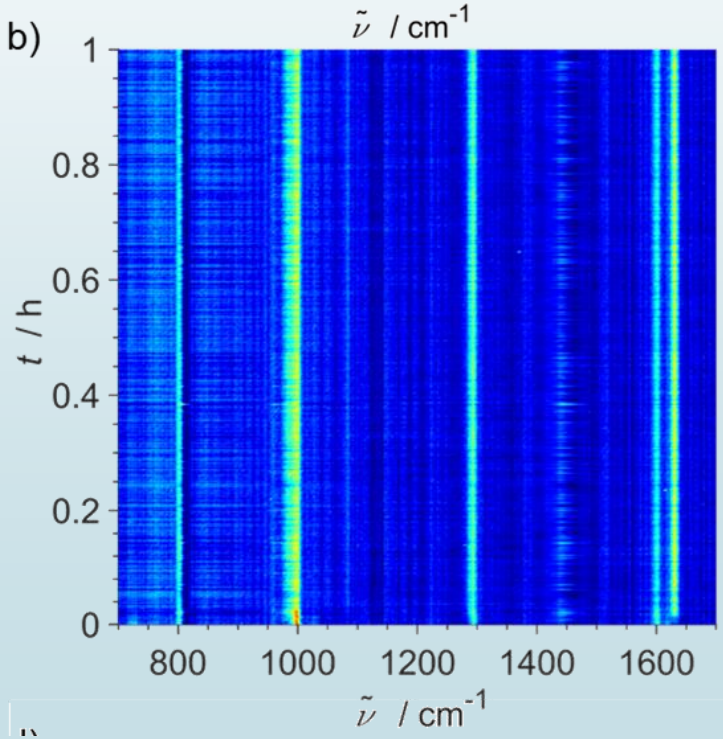


NG (**PBA** : bpy = 3:1)

Mixture of **A31** and **PBA**

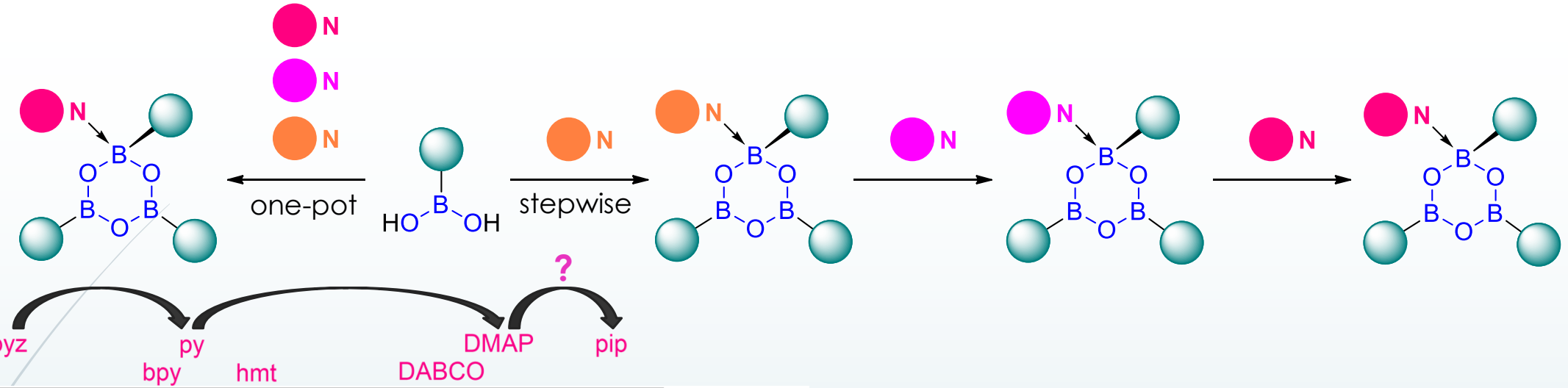


NG (**PBA** : bpy = 6:1)



LAG-MeOH (**PBA** : bpy = 6:1)

mixture



Exchange order depends on the pK_a values of the used amines

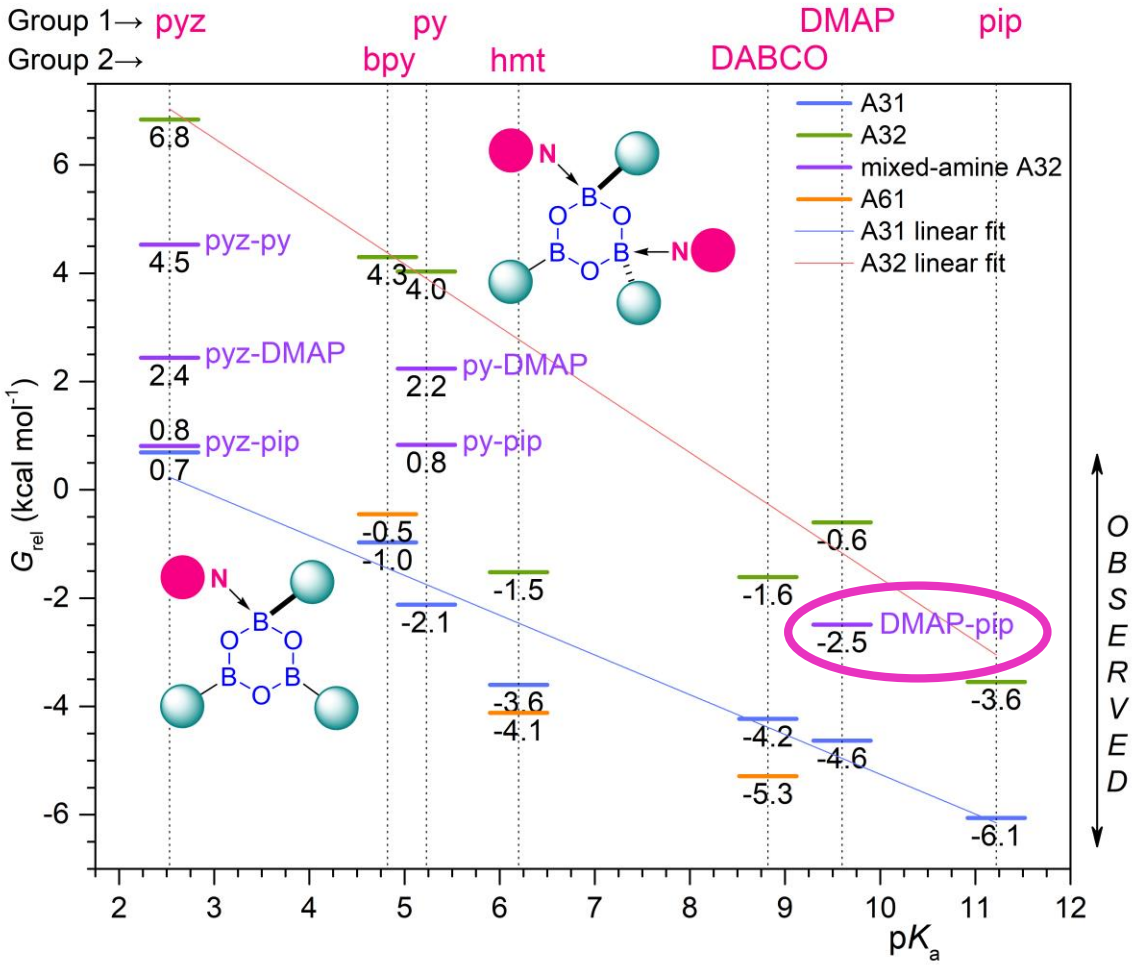
Less basic amine is exchanged with the more basic amine

Works well with the mixture of amines and if more basic amines are added sequentially

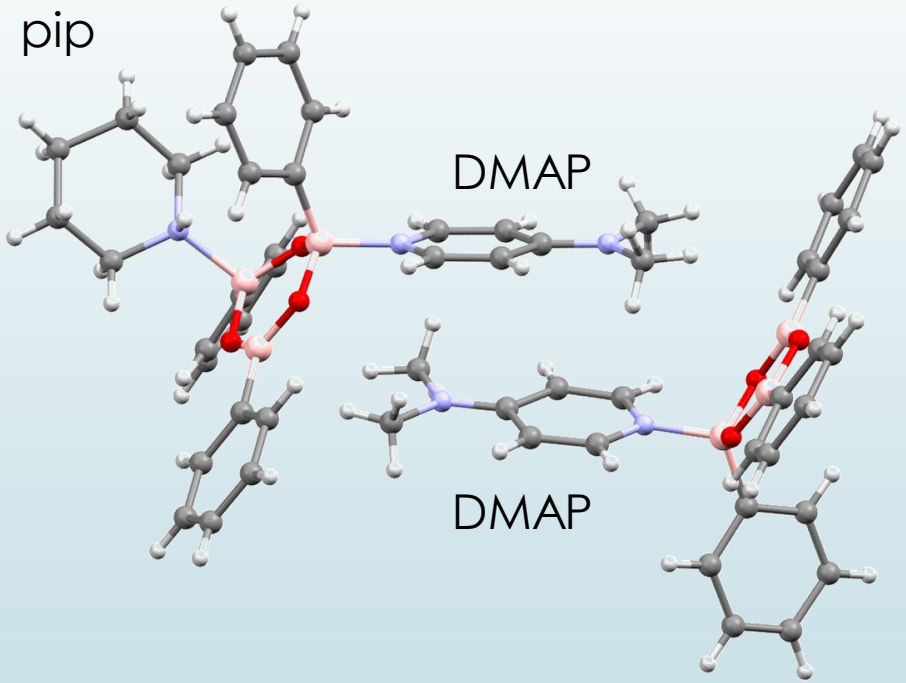
Works for the same structural motif of the B←N adducts

mixture

„Mixed"-amine B←N adducts? Yes!

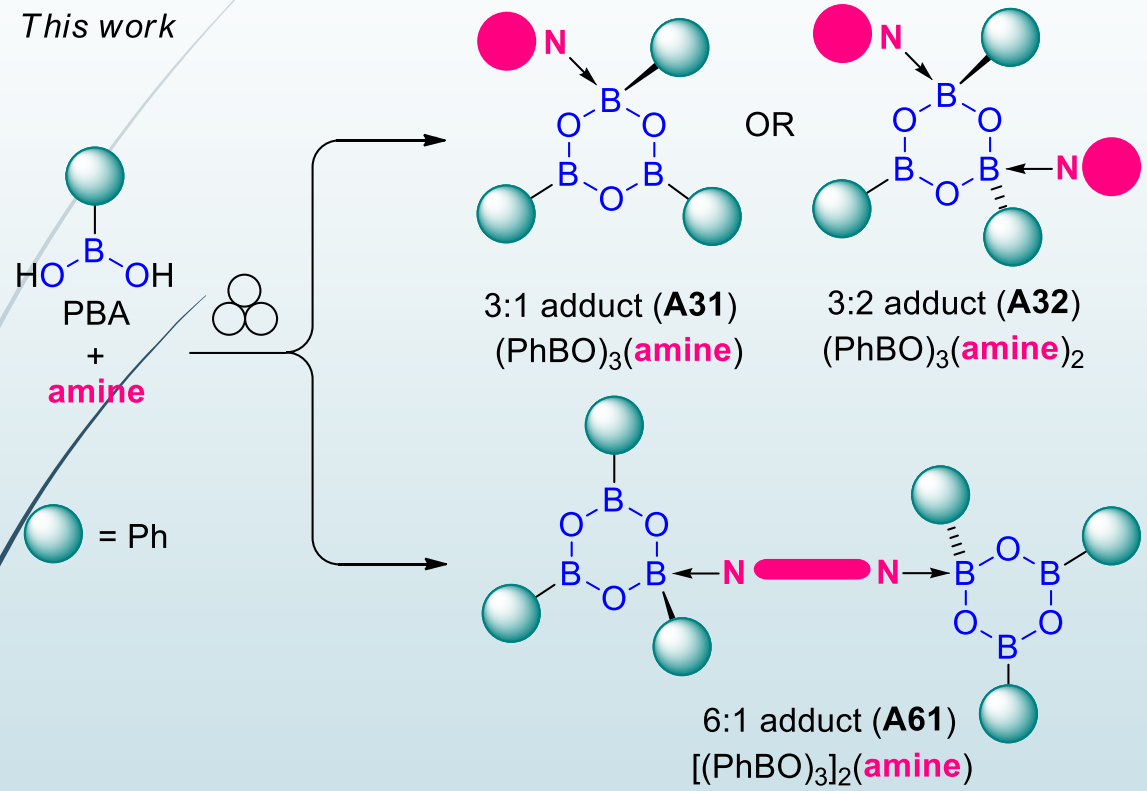


1st isolated „mixed" adduct



$(PhBO)_3$(**DMAP**)(**pip**)·$(PhBO)_3$(**DMAP**)
A32-A31 „mixed" adduct

Conclusion



- **series of amines** used
- **pure B←N adducts** isolated
- **controlled formation** of A31, A32 or A61
- ***in-situ* reaction dynamics**

Chem. Eur. J. **2024**, 30, e202400190.

Calculations used to predict:
- possible products
- the preferred product

and their:
- structure
- Raman spectra

Calculations and experimental endevours worked hand in hand ending in comprehensive understanding of the system

Acknowledgement

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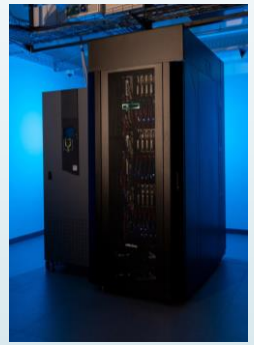
IP-2019-04-9951
DOK-2020-01-7515

Computational resources:

srce | University of Zagreb University Computing Centre

isabella CLUSTER



Supek

Thank you for your attention!