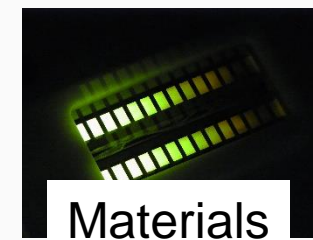
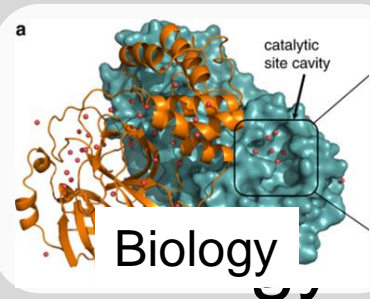


Technologies to accelerate the development of synthetic building blocks for materials sciences

Stefan Bräse group, Nicole Jung (IBCS)

The Compound Platform at KIT



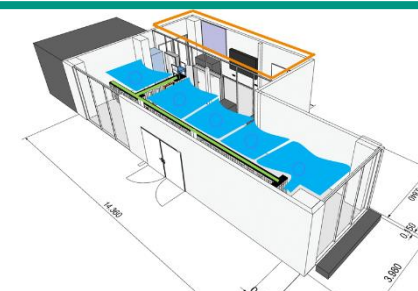
Chemical Synthesis



Molecule Archive

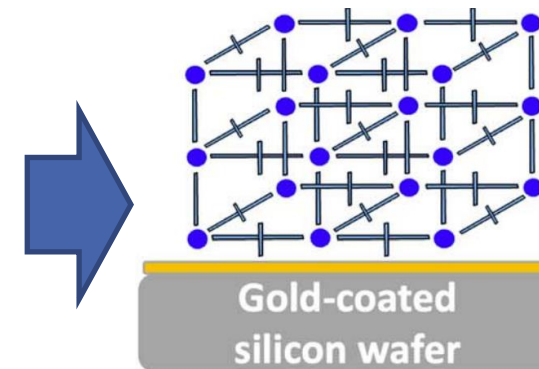
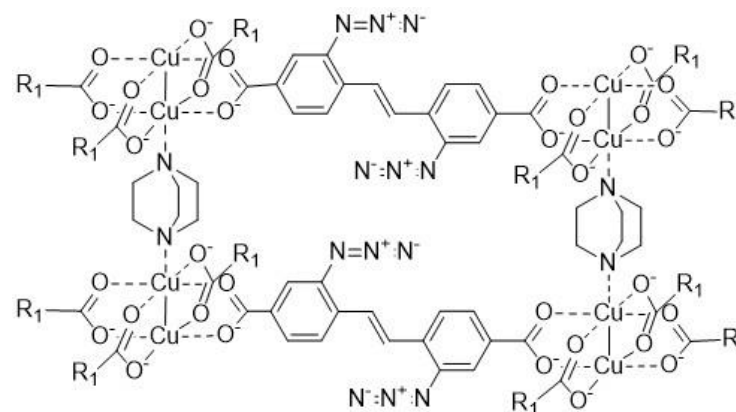
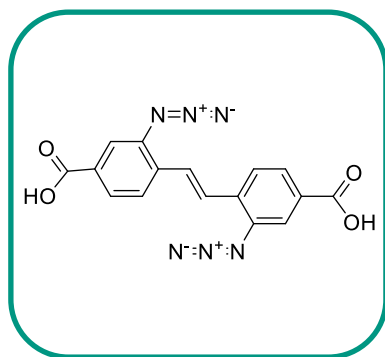


Digitalization

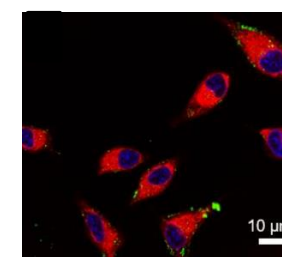
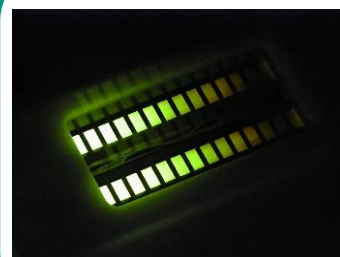
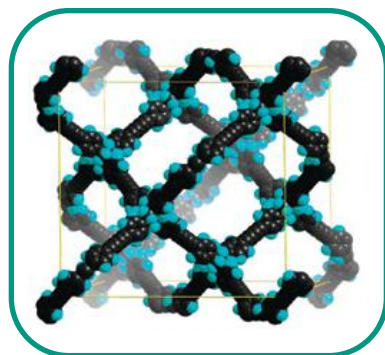


Automation - Robotics

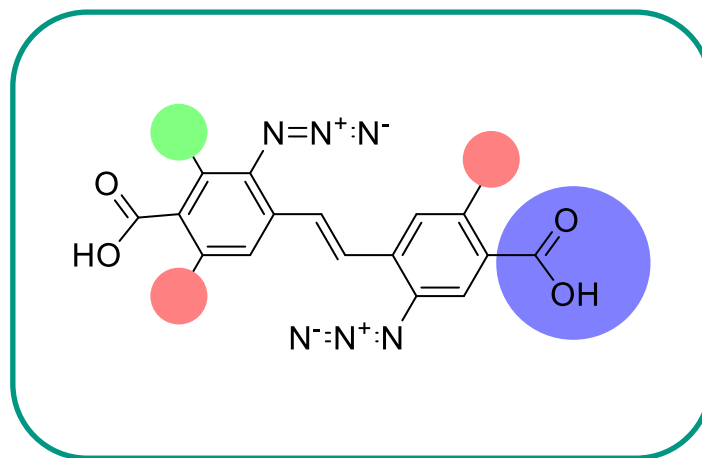
Activities of the Compound Platform



Lena Pilz, Carsten Natzeck, Jonas Wohlgemuth, Nina Scheuermann, Simon Spiegel, Simon Oßwald, Alexander Knebel, Stefan Bräse, Christof Wöll, Manuel Tsotsalas, Nicholas Prasetya, Utilizing machine learning to optimize metal–organic framework-derived polymer membranes for gas separation, *J. Mater. Chem. A* 2023, DOI: [10.1039/D3TA05235D](https://doi.org/10.1039/D3TA05235D)



Steps needed for accelerated processes



Retrosynthesis

Reaction details

Reaction adaptation

Machine readable data

Automation

1

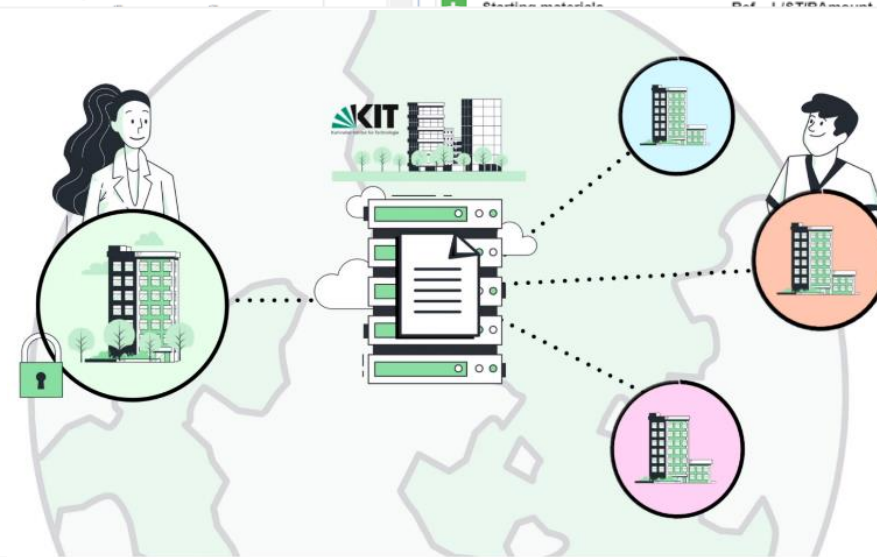
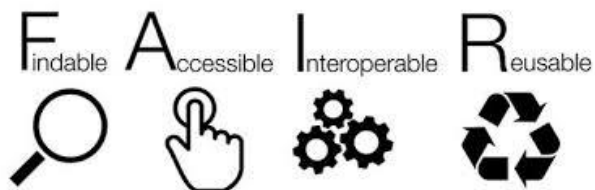
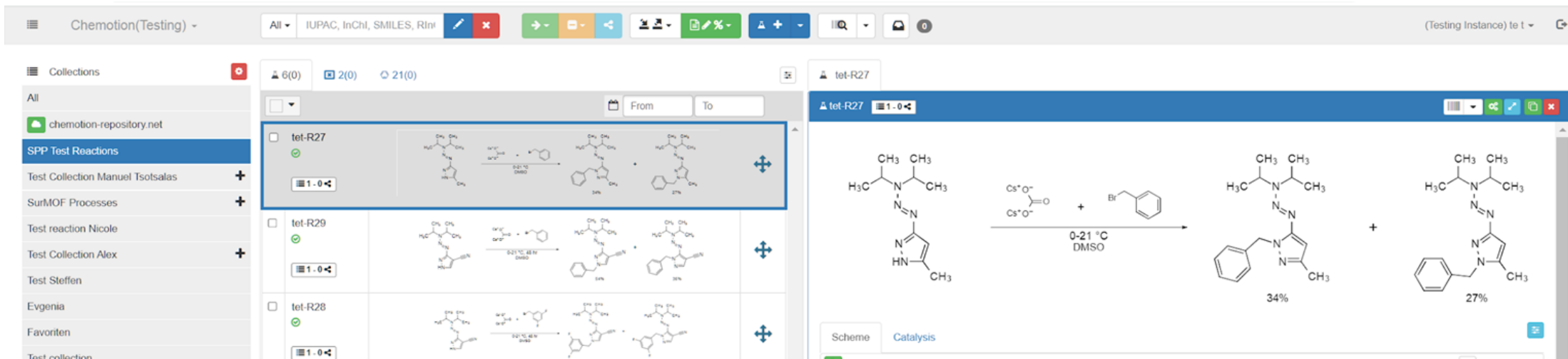
2

3

4

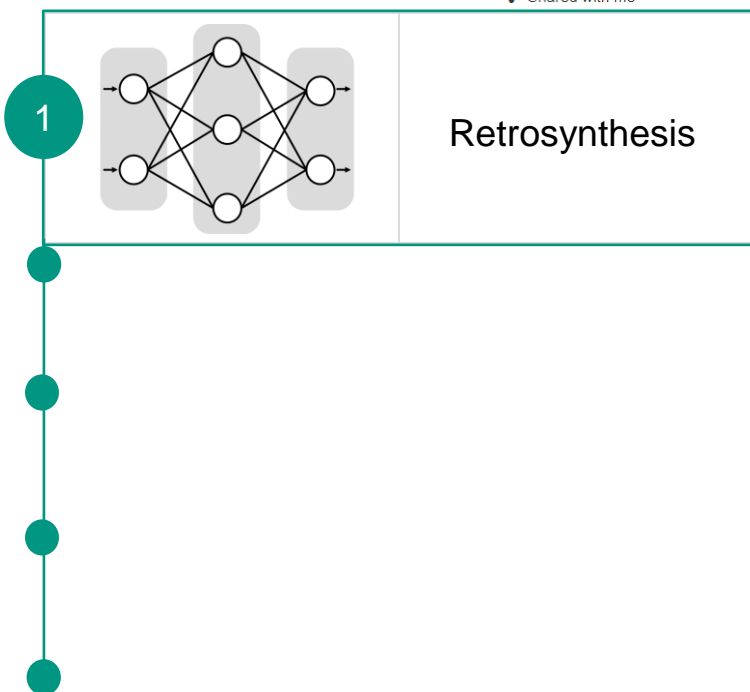
5

Chemotion and LabIMotion used as a framework



LabIMotion
Generic extension

Retrosynthesis – First steps to plan a reaction



Chemotion

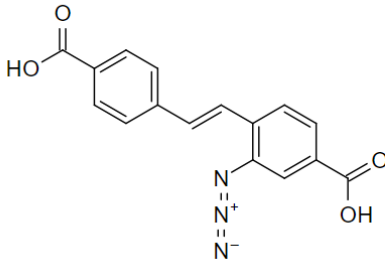
All IUPAC, InChI, SMILES, RInC

Collections

- All
- chemotion-repository.net
- My shared collections
- Shared with me

4(0)

C16H11N3O4



NJ-4

NJ-3

C16H14N2O4

3-amino-4-[(E)-2-(2-amino-4-carboxyphenyl)ethenyl]benzoic acid

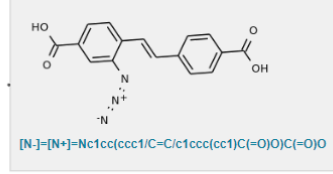
NJ-2

C16H10N6O4

3-azido-4-[(E)-2-(2-azido-4-carboxyphenyl)ethenyl]benzoic acid

NJ-1

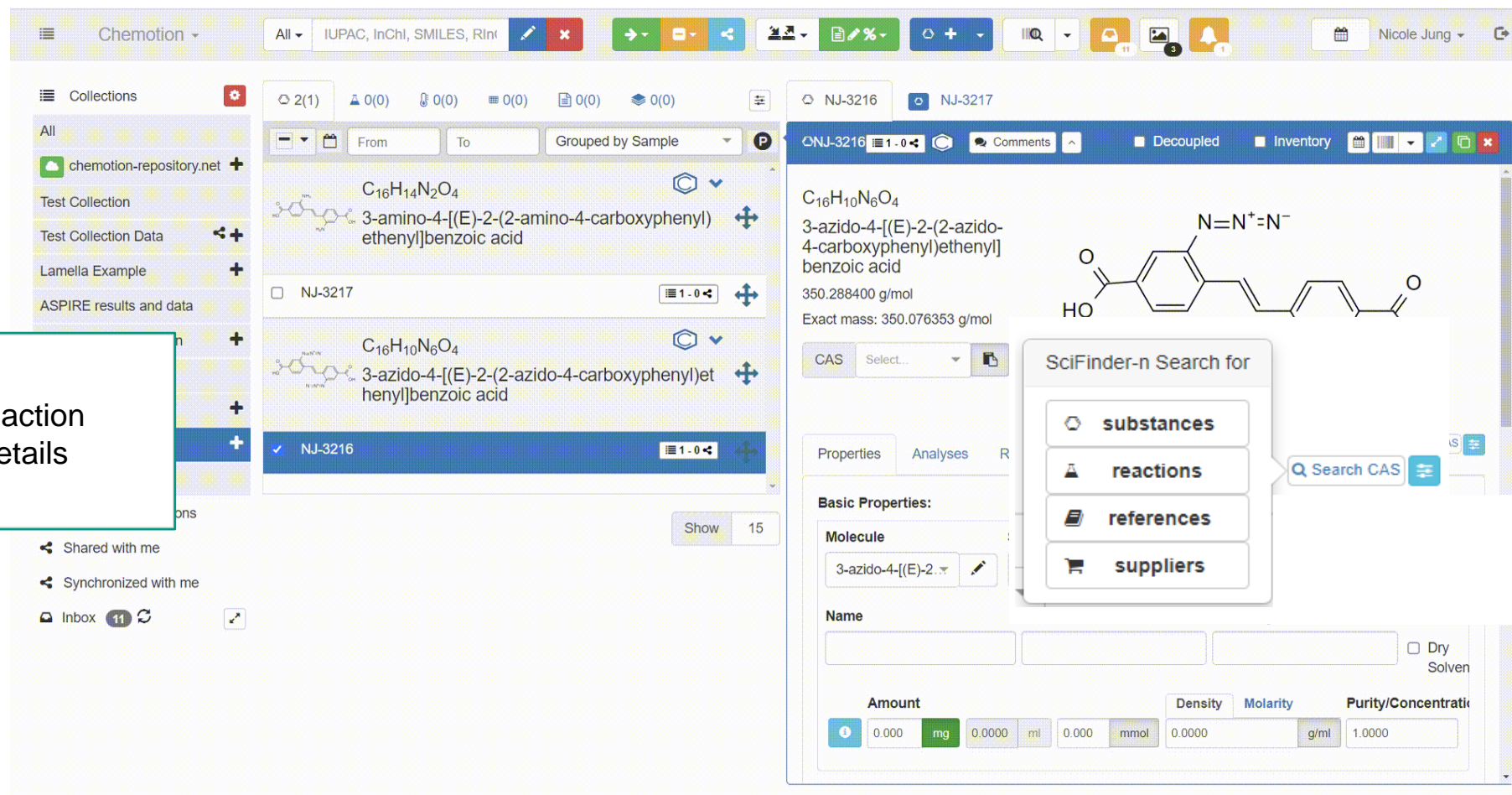
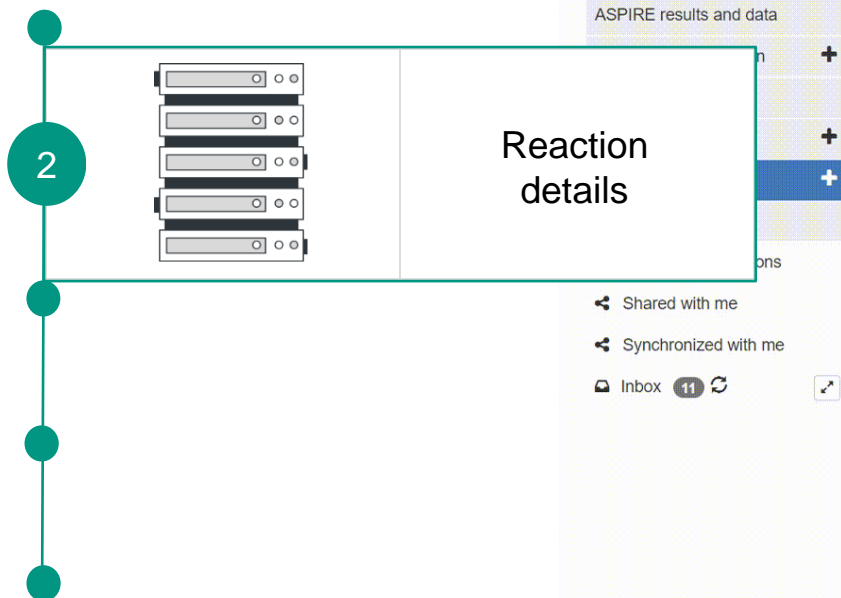
Rank:1



[N-]=[N+]-Nc1cc(ccc1/C=C/c1ccc(cc1)C(=O)O)C(=O)O

Embedded machine learning models for retrosynthesis and reaction prediction: ML developments developed at MIT

Connection to supportive external services

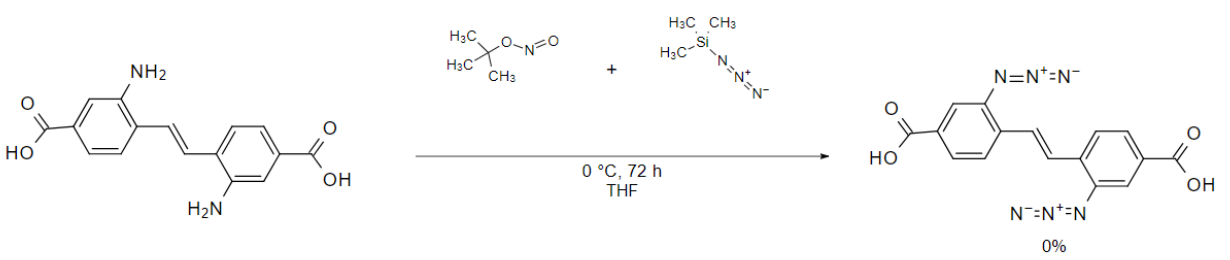


The screenshot displays the Chemotion software interface. On the left, a sidebar shows a 'Collections' menu with options like 'chemotion-repository.net', 'Test Collection', 'Test Collection Data', 'Lamella Example', and 'ASPIRE results and data'. The main area shows a list of chemical samples, including '3-amino-4-[(E)-2-(2-amino-4-carboxyphenyl)ethenyl]benzoic acid' and '3-azido-4-[(E)-2-(2-azido-4-carboxyphenyl)ethenyl]benzoic acid'. A detailed view for sample 'NJ-3216' is shown on the right, featuring its chemical structure, molecular formula $C_{16}H_{10}N_6O_4$, and various properties. A 'SciFinder-n Search for' dropdown menu is open, showing options for 'substances', 'reactions', 'references', and 'suppliers'. The interface also includes a 'Basic Properties' section with fields for 'Molecule', 'Name', 'Amount', 'Density', 'Molarity', and 'Purity/Concentration'.

API connection of external databases such as CAS – SciFinder to query, retrieve and use external content

Reaction planning using different resources

rp-R72 1.0



0 °C, 72 h
THF

0%

Scheme Properties Analyses References Green Chemistry

Starting materials

Ref	L/S	T/R	Coeff	Amount	Conc	Equiv
A NJ-3216-1	s	t	1	167.0 mg	0.00 ml	0.5600 mmol
3-amino-4-[(E)-2-(2-amino-4-carboxyphenyl)ethenyl]benzoic acid						

Reactants

Reagents

L/S	T/R	Coeff	Amount	Conc	Equiv
s	t	1	344.4 mg	0.00 ml	3.340 mmol
s	t	1	256.9 mg	0.00 ml	2.230 mmol

Crude

L/S	T/R	Coeff	Amount	Conc	Yield
s	r	1	0.000 mg	0.00 ml	0.000 mmol

Solvents

DS	T/R	Label	Vol	Vol ratio
s	t	THF	20.0 ml	100.0%

Conditions

Name:

Status:

Temperature: °C

3



Reaction Planning

Reaction planning using different resources

rp-R72 1.0

Scheme Properties Analyses Reference

Starting materials

- NJ-3216-1
- 3-amino-4-[(E)-2-(2-amino-4-carboxyphenyl)]

Reactants

Default solvents

- S1 THF

Name

Name...

Status

Select...

Temperature

0 °C

Start

DD/MM/YYYY hh:mm:ss

Stop

DD/MM/YYYY hh:mm:ss

Duration

Duration

72 Hour(s)

Type (Name Reaction Ontology)

Select...

Role

Select...

Description

Normal

1. Suspend 2,2'-diamino-4,4'-stilbenedicarboxylic acid (0.56 mmol) in dry tetrahydrofuran (20 mL) in a dry 50 mL round-bottom flask.
2. Cool down the suspension to 0 °C.
3. Add *tert*-butylnitrite (0.400 mL, 3.34 mmol, 6 equivalents) dropwise to the solution.
4. Stir the mixture for 15 minutes.
5. Add trimethylsilylazide (0.293 mL, 2.23 mmol, 4 equivalents) dropwise to the mixture at 0 °C.
6. Allow the reaction mixture to room temperature.
7. Stir the reaction mixture for 72 hours.
8. Evaporate tetrahydrofuran under reduced pressure.
9. Treat the crude product with a cold mixture of methanol and tetrahydrofuran (1/1, 20 mL).
10. Filter the crude product.
11. Dry the crude product *in vacuo*

Purification

Filtration

3

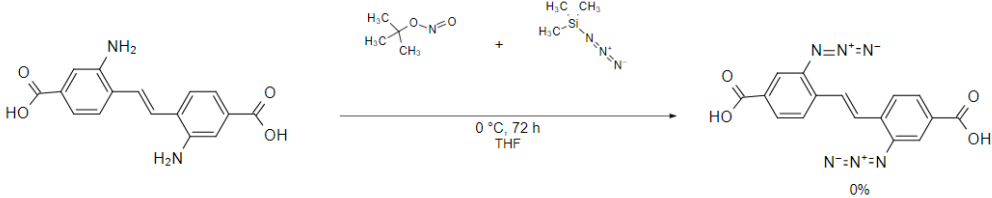


Reaction Planning

From digitalization to automation: machine readability

ELN Process Editor | Collections ▾ Reactions (71) ▾

Reaction: rp-R72
6b0c6e1d-3ee8-46ca-B89d-fb0958f140da



Formula

Preparations

3-amino-4-[(E)-2-(2-amino-4-carboxyphenyl)ethenyl]benzoic acid
Homogenized

+ New Preparation

1/3 Synthese 1

No Vessel assigned

3-amino-4-[(E)-2-(2-amino-4-carboxyphenyl)ethenyl]benzoic acid

Add 3-amino-4-[(E)-2-(2-amino-4-carboxyphenyl)ethenyl]benzoic acid
0.00056 mol
1013 mBar

Add Tert-butyl Nitrite
0.00334 mol
21 °C, 1013 mBar

Add Azido(trimethyl)silane
0.00223 mol
21 °C, 1013 mBar

2/3 Workup

No Vessel assigned

Filtration
FILTRATION
AUTOMATIC
THF

Crystallization
CRYSTALLIZATION
AUTOMATIC

Save
CRUDE rp-116
rp-116

New Action Change Condition

3/3

No Vessel assigned

Transfer
CRUDE rp-116
100 %
From: Workup

Crystallization
CRYSTALLIZATION
AUTOMATIC

New Action Change Condition

+ New Step

4

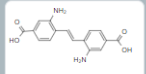
Machine Readable Processes

From digitalization to automation: machine readability

ELN Process Editor | Collections ▾ Rea

Reaction: rp-R72
6b0c6e1d-3ee8-46ca-889d-fb0958f140da

Preparations

3-amino-4-[(E)-2-(2-amino-4-carbo...
 Homogenized

+ New Preparation

object ▸ provenance ▸

object {3}

provenance {4}

experimenter {3}

username : User1 Complat
organization : buggle.net
email : complat.user1@eln.edu
city : Karlsruhe

experimentStart {1}

value : 2023-01-26T11:00:00Z

recordCreated {2}

time {1}

value : 2023-01-04T10:47:22Z

person {3}

username : User1 Complat
organization : buggle.net
email : complat.user1@eln.edu

reactionId : 20c4196b-2794-476b-91f5-d5f1b3a61e0b

reactionSteps {4}

0 {4}

reactionStepId : dc91f99b-9479-453c-ab96-3cc191092d5c

actions {17}

0 {3}

startTime {2}

value : 0
units : SECOND

duration {2}

value : 0
units : SECOND

addition {2}

reactionRole : SOLVENT

input {5}

rp

0° ✎ ⌵

Q

H

✎ ⌵ ⌵

+ New Step

✎ ⌵ ⌵

✎ ⌵ ⌵

4



Machine Readable
Processes

Automation - automated chemical synthesis and analysis



Partner: **KIT - IBCS**
KIT - IFG
KIT - IMT
KIT - IAI
KIT - IMVT

External storage
Part I, capacity: 10.000
automated logistics
Part II, solvent storage

Interface to storage

X-Planar
delivery system based on
magnetic levitation

Sample and vial preparation
evacuation, inert atmosphere
weighing, dosing, liquid handling

Characterization
high field NMR (400 MHz)
Fluorescence

Control area
accessible for employees and visitors
control of the system

Interfaces
interface human accessible area – machines

Processing & reactions
chemical reaction stations, high and low
temperature, diverse conditions and media

In process analysis
GCMS, LCMS
preparation of samples

Media and solvent removal
filtration, evaporation and
lyophilisation

Purification and analysis
preparative purification, HPLC
SFC purification



Automation - automated chemical synthesis and analysis

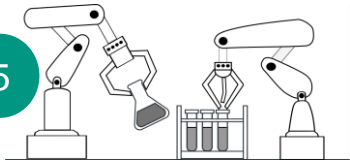


Fluorescence spectrometer	LC prep
NMR spectrometer (400 MHz)	LC-MS analytical scale
GC-MS (Liquid phase analysis)	LC prep (SFC)
GC-BID (Gas phase analysis)	LC-MS analytical scale (type SFC)

Independence of other sites
Setting allows the publication of data without further lab support
Need to embed devices that are not designed for automation
Embedding means software and hardware



5



Automation

Automation - automated chemical synthesis and analysis



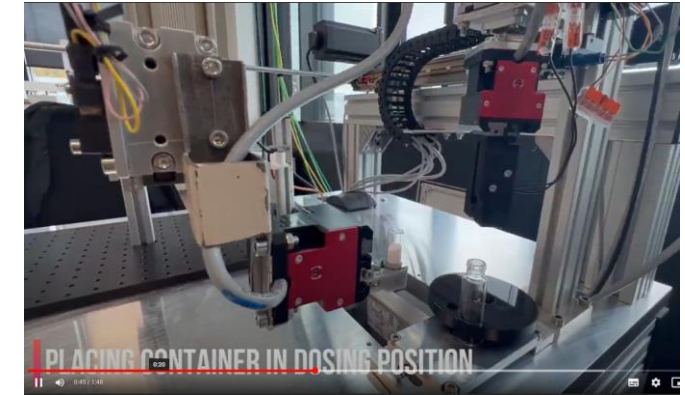
Tile based conveyor
Uses magnetic levitation for transport



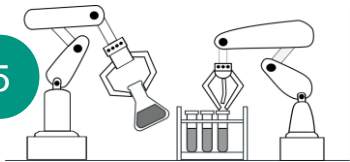
Building smaller devices
Enable automation and parallelization for CO2 reduction



Dosing automation (contact free)
From a few mgs to g scale



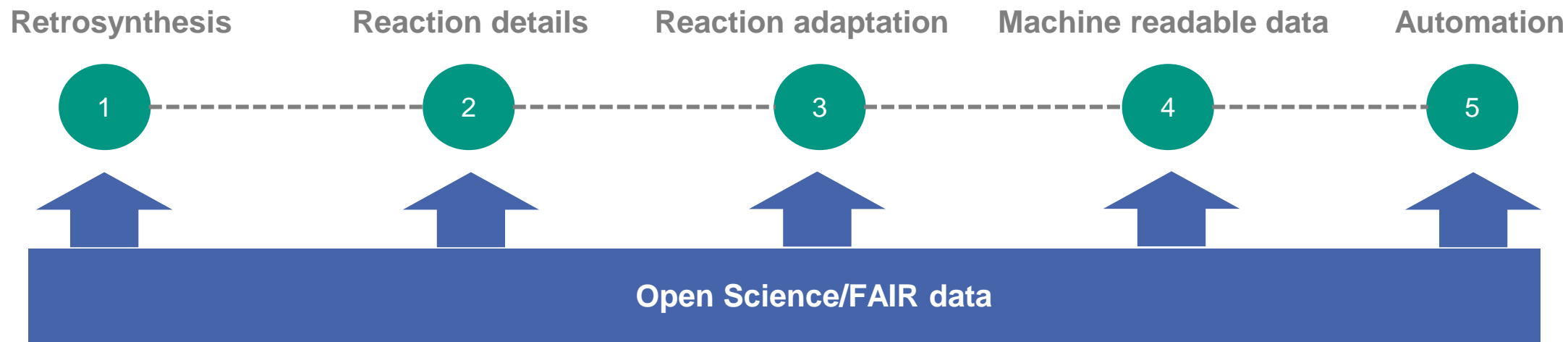
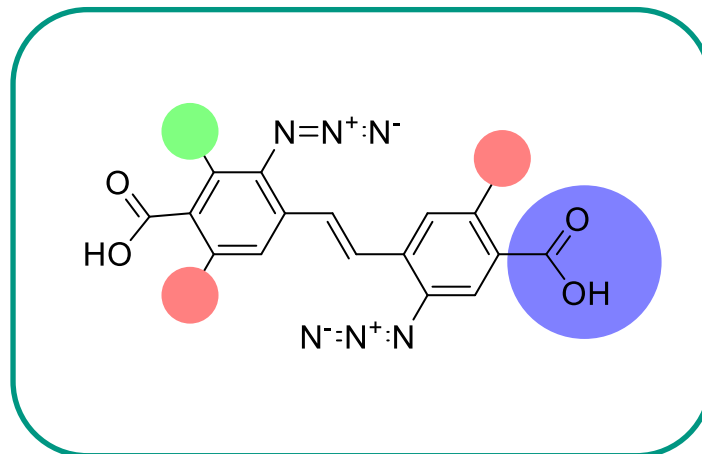
5



Automation

- Open Hardware development and construction
- Open Software concepts wherever possible

Generating data for the next generation of materials



Generating data for the next generation of materials

Chemotion-Repository Data publications Molecule Archive Newsroom How-To LabMotion Login with nicole.jung@kit.edu or Sign Up

Search: IUPAC, InChI, SMILES, ...

by authors: Lena Pilz (LP)

Reactions Samples Scheme-only reactions

Reaction Details:

ID: CRR-35494 **Embargo:** LP_2023-08-25 **Author:** Lena Pilz **Published on:** 2023-09-07 **Analyses:** 1 **X-Vial:** -

Reaction Scheme:

General setting for the synthesis of SURMOFs

Reaction techniques	Processing type	Device	Type of sample holder	No of samples
Dipping	automated	TX-60	4-fold	2

Comments and further Details

Preparation of substrate

Substrate	Coating	Dimensions
Silicon wafer	gold	1x3cm

Activation




SAM	SAM type	Duration
SAM	MHDA (16- Mercaptohexadecanoic acid)	72 h

Preparation of the used chemicals/materials in detail

Table 1: Listing of solvents and definition of solvent mixtures

Solvent label	Solvent A	Volume A	Solvent B	Volume B	Solvent C	Volume C	Ratio [A:B:C]
sol mix 1	EtOH	1340.05 ml	MeOH	129.95 ml		-	10,3:1
sol mix 2	EtOH	178.1 ml	MeOH	17.27 ml		-	10,3:1

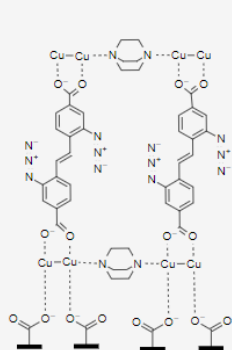
Table 2: Preparation of materials

Vessel No	Vessel Part	Function	Molecule	Method	Solvent label	Volume	Duration	Temperature [°C]
V1	A	metal		sonication	sol mix 1	210 ml	20 m	25
V2	A	cleaning agent		none	sol mix 1	210 ml	-	25
V3	A	cleaning agent		none	sol mix 1	210 ml	-	25
V4	A	cleaning agent		none	sol mix 1	210 ml	-	25
V5	A	linker		sonication	sol mix 2	195.37 ml	20 m	25
V5	B	modulators		sonication	sol mix 2	195.37 ml	20 m	25

Generating data for the next generation of materials

Q All IUPAC, InChI, SMILES, ...

(Sur)MOF Reaction



Viewer

Product

Formula: $C_{51}H_{49}Cu_8N_{16}O_{16}$

Canonical SMILES: C1CN2CCN1CC2.C1CN2CCN1CC2.[O-]C(=O)C.[O-]C(=O)C.[O-]C(=O)C.[O-]C(=O)C.[N-]=[N+]=Nc1ccc(cc1/C=C/c1ccc(cc1N=[N+]=[N-])C(=O)[O-])C(=O)[O-].[N-]=[N+]=Nc1ccc(cc1/C=C/c1ccc(cc1N=[N+]=[N-])C(=O)[O-])C(=O)[O-].[Cu][Cu].[Cu][Cu].[Cu][Cu].[Cu][Cu]

InChI: InChI=1S/2C16H10N6O4.2C6H12N2.4C2H4O2.8Cu/c2*17-21-19-13-7-11(15(23)24)5-3-9(13)1-2-10-4-6-12(16(25)26)8-14(10)20-22-18;2*1-2-8-5-3-7(1)4-6-8;4*1-2(3)4;...../h2*1-8H,(H,23,24)(H,25,26);2*1-6H2,4*1H3,(H,3,4);...../p-8/b2*2-1+.....

InChIKey: DBLYDXDFRQUSRQ-QYQCSXRTSA-F

Exact Mass: 1644.776980 g·mol⁻¹

Sample DOI: [10.14272/DBLYDXDFRQUSRQ-QYQCSXRTSA-F.29](https://doi.org/10.14272/DBLYDXDFRQUSRQ-QYQCSXRTSA-F.29)

JSON-LD

Sample ID: CRS-35862

Reference in the Literature:

(Sur) MOF Details

(SUR)MOF configuration

List of (ionic) (SUR)MOF fragments

☐

SURMOF

☒

substrate

Silicon

coating

Gold

dimensions

1x3cm

Format ID

MOFid-v1

Format Key

MOFkey-v1

Topology Code(s)

pcu

Catenation

cat0

Comments

<https://doi.org/10.1021/acs.cgd.001050>

CCDC No

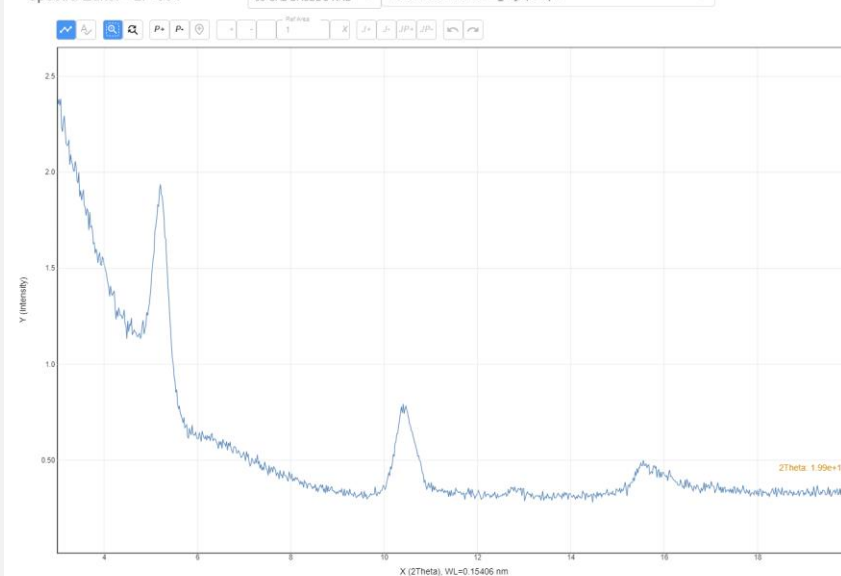
001050

MOF identifier

C1CN2CCN1CC2.[Cu][Cu].[N-]=[N+]=Nc1ccc(cc1C=Cc1ccc(cc1N=[N+]=[N-])C(=O)[O-])C(=O)[O-]


Spectra Editor - LP-554

08-GA2-DASBDC-XRD 08-GA2-DASBDC-Pos.1.1_bagit peak.idx



Info

Title: 08-GA2-DASBDC-Pos.1.1_bagit



Spectra Comparisons

Thank you for listening

