

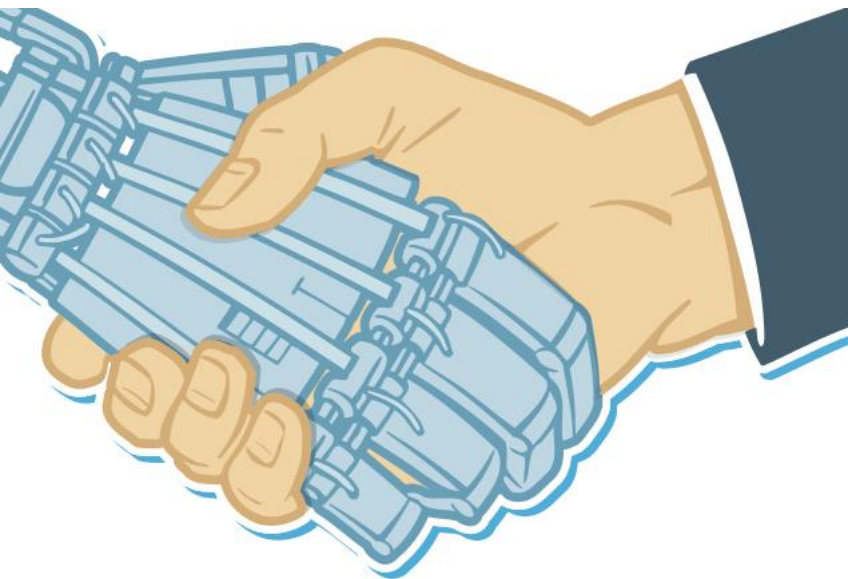
CHEMCURATOR & MARKUSH WORLD

Árpád Figyelmesi
Budapest Annual Meeting
2016



CHEMCURATOR

Computer-assisted chemical data extraction



- English, Chinese and Japanese N2S
- Markush Editor
- Structure Checker
- Search and representation

Compounds extraction view

Project explorer

- US20090048306A1
- US20090270418A1
- US6756383_DEMO
- Markush
- Structures [21 structures]

Annotated document

US6756383_DEMO

The following mixture was allowed to warm to room temperature overnight. The mixture was quenched with NH_4Cl (aqueous saturated solution) and extracted with EtOAc . The organic layer washed with H_2O and brine, dried over Na_2SO_4 , filtered, and concentrated in vacuo to yield a brown solid. The crude material was purified by column chromatography (10% EtOAc in hexane) to yield the desired product. LC/MS m/z 278.3 (MH+), R_f 1.88 minutes.

3,4-bipyridin-2-one

ethyl 2-(5-methylbenzimidazol-2-yl)acetamide (1.0 eq) was heated in NaOMe (18 eq, 0.5 M in MeOH) at 70° C. for 2 and the resulting solid was filtered and washed with water to provide the desired product. LC/MS m/z 278.3 (MH+), R_f 1.91 minutes.

Example 4

Ethyl 2-(5-methylbenzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 3, Method A using ethyl 2-(5-methylbenzimidazol-2-yl)acetate. LC/MS m/z 292.4 (MH+), R_f 1.71 minutes.

N-(4-Cyano(3-pyridyl))-2-(5-methylbenzimidazol-2-yl)acetamide

The title compound was synthesized as described in Example 3, Method A using ethyl 2-(5-methylbenzimidazol-2-yl)acetate. LC/MS m/z 292.4 (MH+), R_f 1.71 minutes.

4-Amino-3-(5-methylbenzimidazol-2-yl)hydropyridino[3,4-b]pyridin-2-one

The title compound was synthesized as described in Example 3, Method A using N-(4-cyano(3-pyridyl))-2-(5-methylbenzimidazol-2-yl)acetamide. LC/MS m/z 292.4 (MH+), R_f 2.04 minutes.

Example 5

4-(2-Morpholin-4-ylethoxy)-2-nitrophenylamine

Diisopropyl azodicarboxylate (1.1 eq) was added dropwise to a stirred solution of 4-amino-3-nitrophenol (1.0 eq), tris(hydroxymethyl)aminomethane (1.0 eq) and N,N -dimethylmorpholine (1.0 eq) in THF at 0° C. The mixture was allowed to warm to

Selected structures

Compound list

#	Structure	Formula	Mass	Name	Comments
1				4-amino-3-(5-methylbenzimidazol-2-yl)-1H-1,7-naphthyridin-2-one	Ester in Y
2		C16H12N4O2	292.30	4-hydroxy-3-(5-methyl-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	OH in Y p
3		C15H11N5O	277.29	4-amino-3-(1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
4		C16H13N5O	291.31	4-amino-3-(5-methyl-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
5		C21H22N6O3	406.45	4-amino-3-(5-[2-(morpholin-4-yl)ethoxy]-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
6		C18H16N6O2	348.37	2-(4-amino-2-oxo-1H-1,7-naphthyridin-3-yl)-N,N-dimethyl-1H-1,7-naphthyridin-2-one	

Compounds extraction view

ChemCurator 15.5.4

File Edit View Tools Window Help

Projects [21 structures]

US6756383_DEMO

3-(1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-4-yl 3-(... Ester in Y

The reaction mixture was allowed to warm to room temperature overnight. The mixture was quenched with NH₄Cl (aqueous saturated solution) and extracted with EtOAc. The organic layer washed with H₂O and brine, dried over Na₂SO₄, filtered, and concentrated in vacuo to yield a brown solid. The crude material was purified by silica gel chromatography (5:1 EtOAc:hexane) to yield the desired product. LC/MS m/z 278.3 (MH⁺), R_f 1.88 minutes.

4-Amino-3-benzimidazol-2-ylhydropyridino[3,4-b]pyridin-2-one

2-Benzimidazol-2-yl-N-(4-cyano(3-pyridyl))acetamide (1.0 eq) was heated in NaOMe (18 eq, 0.5 M in MeOH) at 70° C. for 2 hours. The reaction mixture was cooled, and the resulting solid was filtered and washed with water to provide the desired product. LC/MS m/z 278.3 (MH⁺), R_f 1.91 minutes.

Example 4

Ethyl 2-(5-methylbenzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 3 using 4-methyl-1,2-phenylenediamine. LC/MS m/z 219.3 (MH⁺), R_f 1.60 minutes.

N-(4-Cyano(3-pyridyl))-2-(5-methylbenzimidazol-2-yl)acetamide

The title compound was synthesized as described in Example 3, Method A using ethyl 2-(5-methylbenzimidazol-2-yl)acetate. LC/MS m/z 292.4 (MH⁺), R_f 1.71 minutes.

4-Amino-3-(5-methylbenzimidazol-2-yl)hydropyridino[3,4-b]pyridin-2-one

The title compound was synthesized as described in Example 3, Method A using N-(4-cyano(3-pyridyl))-2-(5-methylbenzimidazol-2-yl)acetamide. LC/MS m/z ... (MH⁺), R_f 2.04 minutes.

Example 5

4-(2-Morpholin-4-ylethoxy)-2-nitrophenylamine

Diisopropyl azodicarboxylate (1.1 eq) was added to a stirred solution of 4-amino-3-nitrophenol (1.0 eq), tris(hydroxymethyl)aminomethane (1.0 eq) and N,N'-bis(trimethylammonium)ethylenediamine (1.0 eq) in THF at 0° C. The mixture was allowed to warm to

Checker View [There are no problems found.]

Fix All + Fix Selected

Structures

#	Structure	Formula	Mass	Name	Commen
1		C29H18N6O6	498.46	3-(1H-1,3-benzodiazol-2-yl)-2-oxo-1H-1,7-naphthyridin-4-yl 3-(... Ester in Y	
2		C16H12N4O2	292.30	4-hydroxy-3-(5-methyl-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	OH in Y p
3		C15H11N5O	277.29	4-amino-3-(1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
4		C16H13N5O	291.31	4-amino-3-(5-methyl-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
5		C21H22N6O3	406.45	4-amino-3-(5-[2-(morpholin-4-yl)ethoxy]-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
6		C18H16N6O2	348.37	2-(4-amino-2-oxo-1H-1,7-naphthyridin-3-yl)-N,N-dimethyl-1H-1,2,3-triazol-4-amine	

Compounds extraction view

ChemCurator 15.5.4

File Edit View Tools Window Help

Projects [US6756383_DEMO]

US20090048306A1
US20090270418A1
US6756383_DEMO
Markush
Structures [21 structures]

US6756383_DEMO

4-Amino-3-benzimidazol-2-ylhydropyridino[3,4-b]pyridin-2-one

2-Benzimidazol-2-yl-N-(4-cyano(3-pyridyl))acetamide (1.0 eq) was heated in NaOMe (18 eq, 0.5 M in MeOH) at 70° C. for 2 hours. The reaction mixture was cooled, and the resulting solid was filtered and washed with water to provide the desired product. LC/MS m/z 278.3 (MH+), R_t 1.91 minutes.

Example 4

Ethyl 2-(5-methylbenzimidazol-2-yl)acetate

The title compound was synthesized as described in Example 3 using 4-methyl-1,2-phenylenediamine. LC/MS m/z 219.3 (MH+), R_t 1.60 minutes.

N-(4-Cyano(3-pyridyl))-2-(5-methylbenzimidazol-2-yl)acetamide

The title compound was synthesized as described in Example 3, Method A using ethyl 2-(5-methylbenzimidazol-2-yl)acetate. LC/MS m/z 292.4 (MH+), R_t 1.71 minutes.

4-Amino-3-(5-methylbenzimidazol-2-yl)hydropyridino[3,4-b]pyridin-2-one

The title compound was synthesized as described in Example 3, Method A using N-(4-cyano(3-pyridyl))-2-(5-methylbenzimidazol-2-yl)acetamide. LC/MS m/z 292.4 (MH+), R_t 2.04 minutes.

Example 5

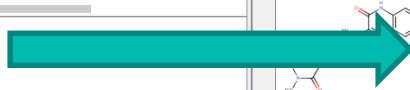
4-(2-Morpholin-4-ylethoxy)-2-nitrophenylamine

Diisopropyl azodicarboxylate (1.1 eq) was added dropwise to a stirred solution of 4-amino-3-nitrophenol (1.0 eq), triphenylphosphine (1.1 eq), and N,N'-bis(2-hydroxyethyl)morpholine (1.0 eq), in THF at 0° C. The mixture was allowed to warm to

Checker View [There are no problems found.]

Fix All + Fix Selected

#	Structure	Formula	Mass	Name	Commer
1		C25H18N6O6	498.46	3-(1H-1,3-benzodiazol-2-yl)-2-oxo-1H-1,7-naphthyridin-4-yl 3-oxopropanoate	Ester in Y
2		C16H12N4O2	292.30	4-hydroxy-3-(5-methyl-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	OH in Y p
3		C15H11N5O	277.29	4-amino-3-(1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
4		C16H13N5O	291.31	4-amino-3-(5-methyl-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
5		C21H22N6O3	406.45	4-amino-3-([2-(morpholin-4-yl)ethoxy]-1H-1,3-benzodiazol-2-yl)-1H-1,7-naphthyridin-2-one	
		C18H16N6O2	348.37	2-(4-amino-2-oxo-1H-1,7-naphthyridin-3-yl)-N,N-dimethyl-1H-1,2,3-triazol-4-amine	



Markush extraction view

Annotated document

Structure Checker

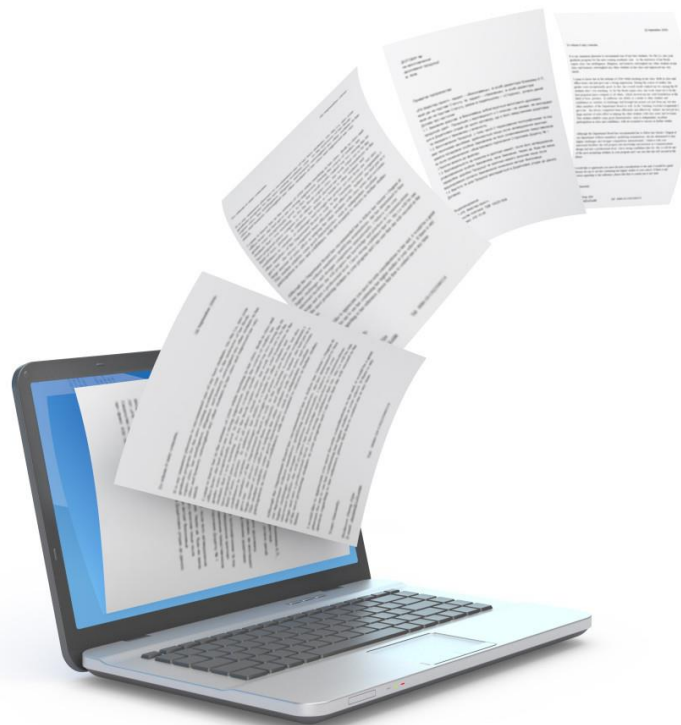
Selected structures

Markush Editor

Example structures

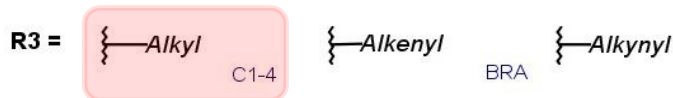
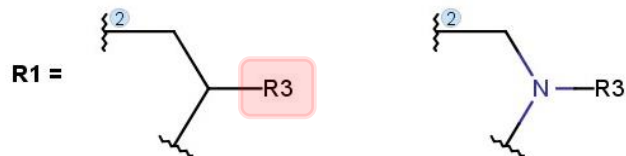
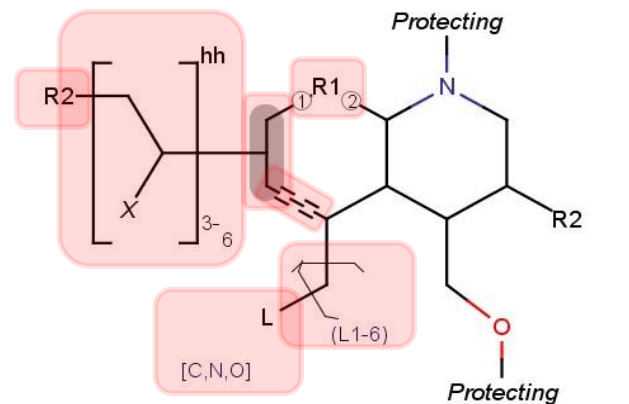
General document curation

- Files (XML, PDF, HTML)
- Google Patents
- IFI CLAIMS
- Images (CLiDE & OSRA)



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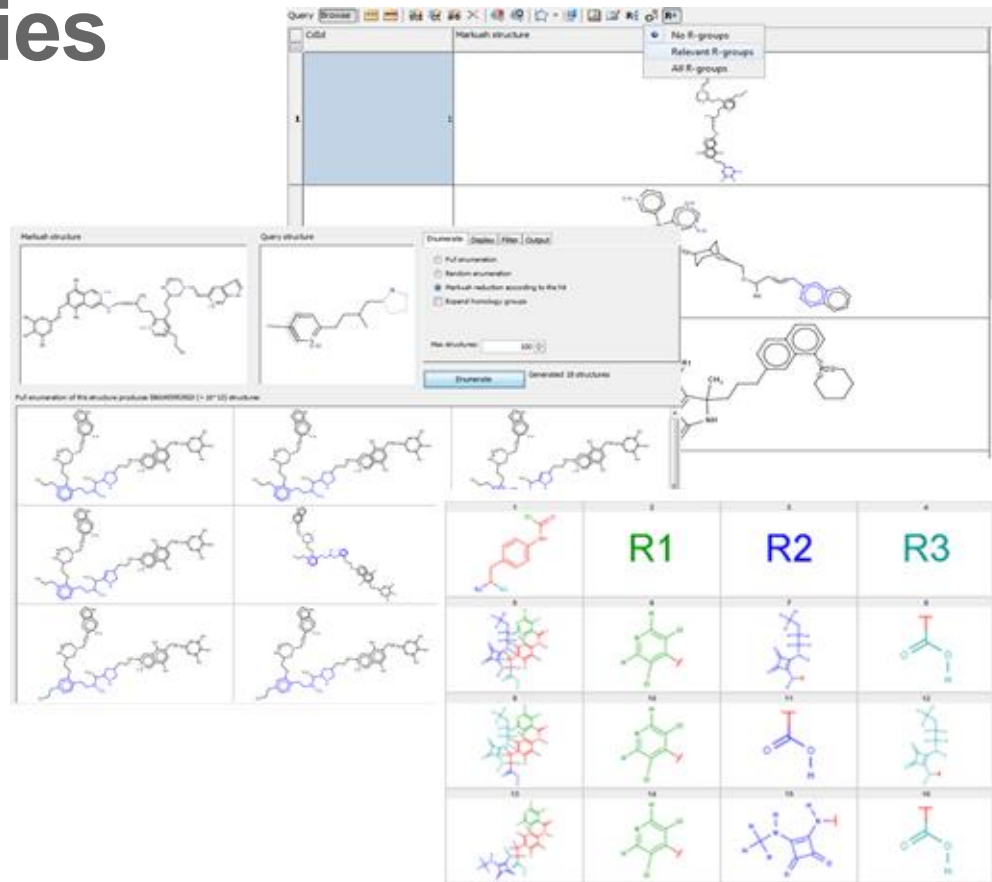
Markush Representation



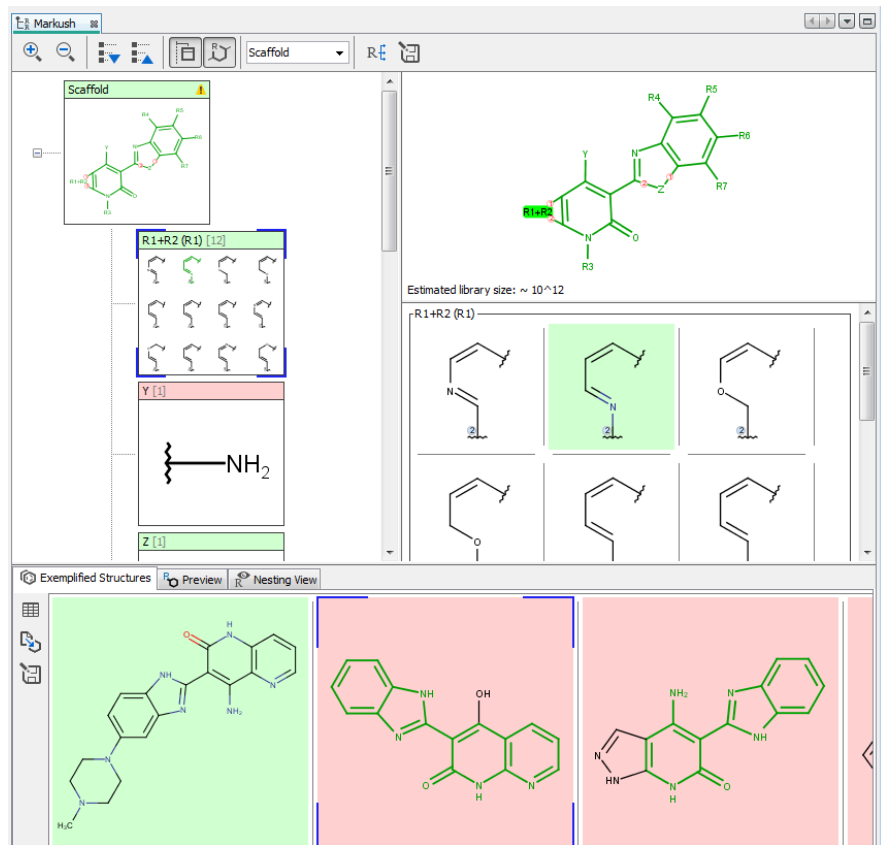
- R-groups
- Atom lists
- Bond lists
- Position variations
- Link nodes
- Repeating units
- Homology groups

Markush technologies

- Search
- Enumeration
- Hit visualization
- Non-hit visualization
- Overlap
- Composer



Non-hit visualization



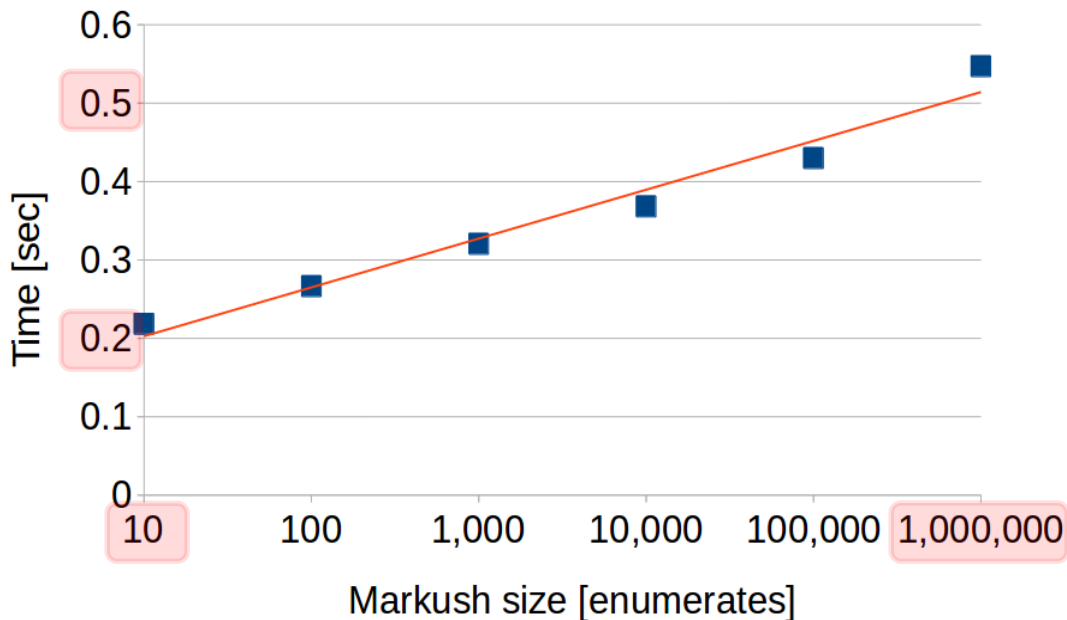
Differentiating structure parts visualization in target Markush and Query structure.

Based on Markush Overlap and MCS technologies

Benefits:

- No enumeration
- No size limitations

Markush Overlap



Overlapping chemical space calculation

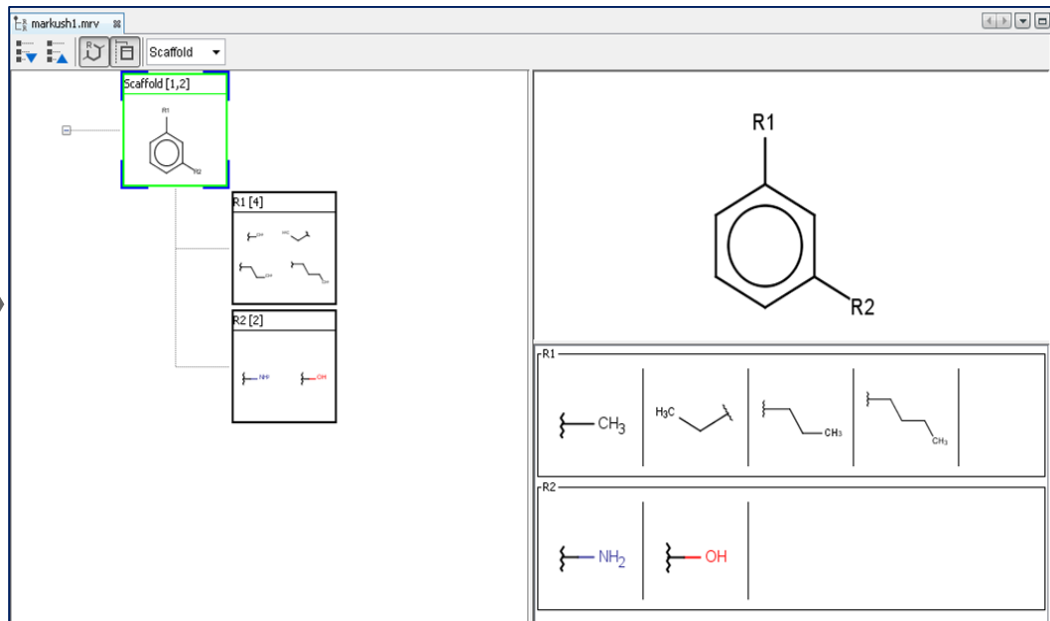
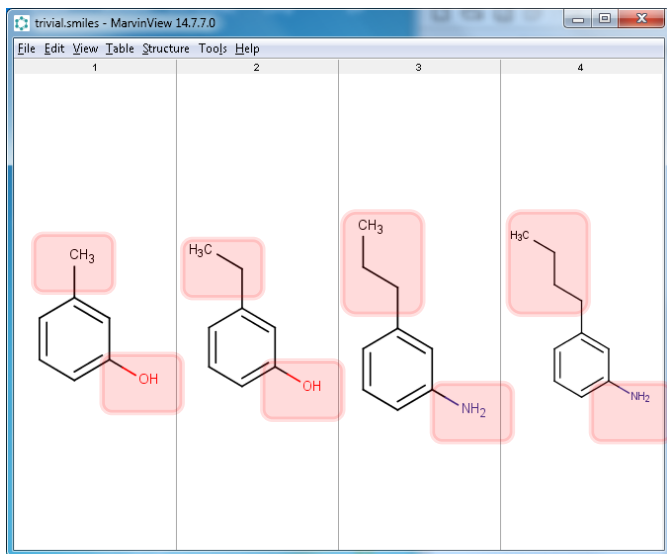
Results:

- Percentage of overlap
- Overlapping Markush

Benefits:

- No enumeration
- No size limitations

Markush Composer



Combinatorial or Patent Markush generation

THANK YOU