

Creating and understanding Markush libraries

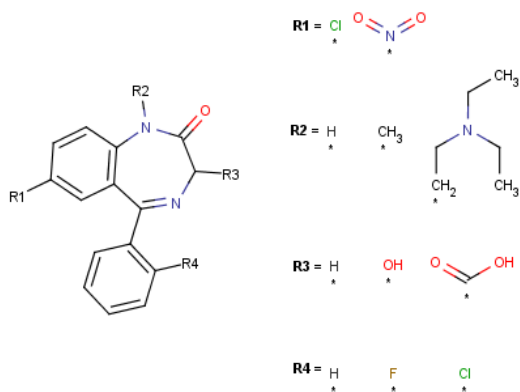
The New Markush Editor

Árpád Figyelmesi



Motivation

Markush structures are widely used in combinatorial chemistry and patents to define large chemical spaces.



United States Patent [19]
 Bitonti et al.

[11] **Patent Number:** 5,681,863
 [45] **Date of Patent:** Oct. 28, 1997

[54] **NON-METABOLIZABLE CLOMIPHENE ANALOGS FOR TREATMENT OF TAMOXIFEN-RESISTANT TUMORS**

[75] Inventors: **Alan J. Bitonti**, Maineville; **Russell J. Baumann**, Cincinnati, both of Ohio

[73] Assignee: **Merrell Pharmaceuticals Inc.**, Cincinnati, Ohio

[21] Appl. No.: **350,192**

[22] Filed: **Dec. 5, 1994**

Related U.S. Application Data

[62] Division of Ser. No. 196,817, Feb. 10, 1994, Pat. No. 5,410,080, which is a continuation of Ser. No. 945,305, Sep. 15, 1992, abandoned.

[51] **Int. Cl.**⁵ **A61K 31/135**

[52] **U.S. Cl.** **514/648; 514/649**

[58] **Field of Search** **514/648, 649**

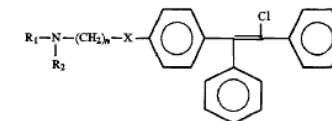
[56] **References Cited**

3,631,109 12/1971 O'Sega et al. 260/570.9
 4,696,949 9/1987 Toivola et al. 514/644
 4,839,155 6/1989 McCague 514/651
 5,114,951 5/1992 King et al. 514/290
 5,130,424 7/1992 Weintraub 540/28

Primary Examiner—Jerome D. Goldberg
Attorney, Agent, or Firm—Nelsen L. Lentz

[57] **ABSTRACT**

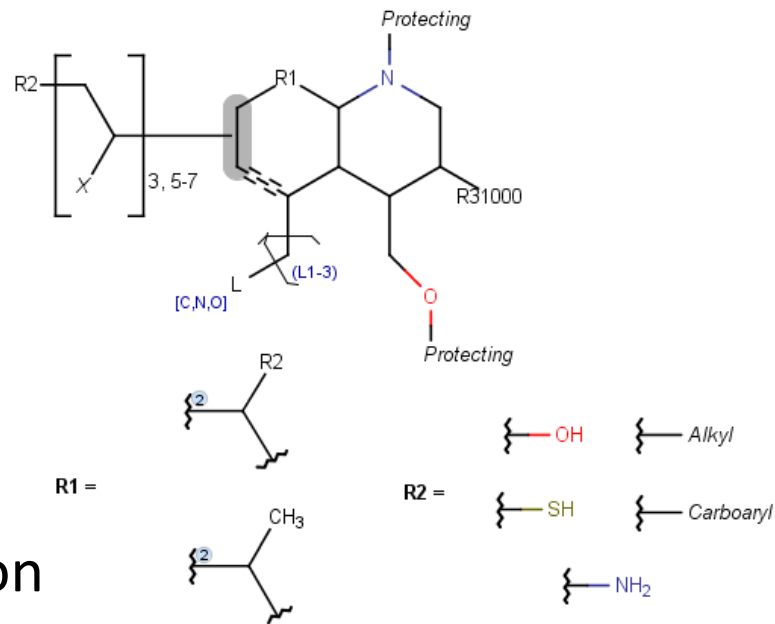
Compounds of the formula:



wherein R_1 and R_2 are each selected from the group consisting of C_1-C_2 lower alkyl; X is NH or S; and n is a whole number within the range of 1-4 inclusive; and when n=0, X is $(CH_2)_3$ and the pharmaceutically acceptable salts thereof

Overview

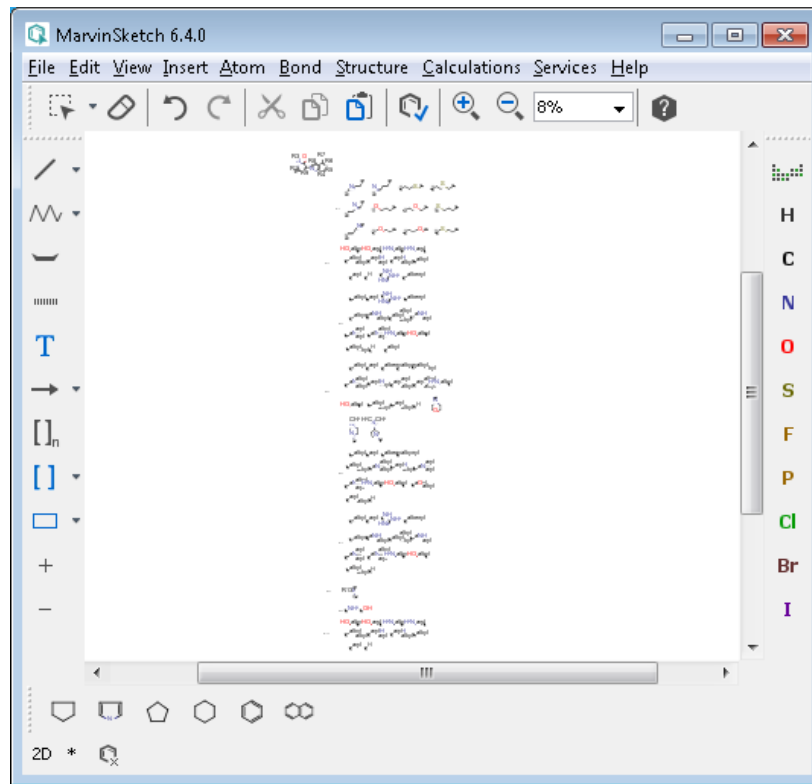
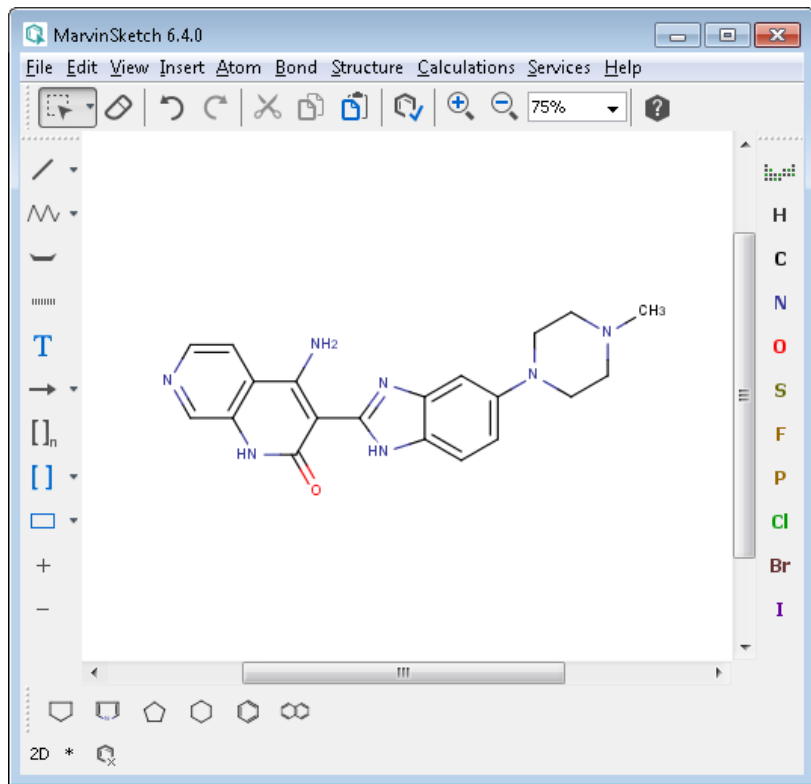
- Market leader Markush technology
 - R-groups
 - Atom lists, bond lists
 - Position variation bond
 - Link nodes
 - Repeating units
 - Homology groups
- Markush enumeration
- Markush search & hit visualization
- R-group decomposition



Challenges

- No proper tools for editing complex Markush structures
- Manual processing and analyzing is time consuming and needs special expertise

General structure editors



Markush Editor

- Editing complex patent Markush structures
- Hierarchical representation of fragments' relationships
- Visualization of nesting view, preview
- Editing individual fragments separately
- Integrated structure checker
- Available as a desktop application and as an integratable component

Markush Editor

The screenshot displays the Markush Editor interface with several key components highlighted by callouts:

- Structure checker:** Located in the top-left pane, it lists error types such as "Overlapping Atoms Checker" (3 overlapping atoms found) and "R-group Attachment Error Checker" (1 R-group has attachment error).
- Scaffold:** A callout points to the main chemical structure in the top-right pane, which is a complex multi-ring system with various substituents labeled R1 through R9.
- Tree view:** A callout points to the hierarchical tree structure in the center, showing the nesting of R-groups (R1, R3, R4) and their associated chemical fragments.
- R-group definitions:** A callout points to the bottom-right pane, which defines R-groups like "alkyl", "alkenyl", and "aryl" with their respective chemical structures and symbols.
- Nesting view & Preview:** A callout points to the bottom section, which shows the "Nesting view" of the structure and a "Preview" of the resulting chemical structures after R-group substitution.

Coming soon in Markush Editor

- Markush composer function
- New Markush structure checker functions
- Markush standardization
- Alias handling

Coming soon in Markush technology

- Markush overlap analysis
Percentage of overlap and representation of overlapping chemical space
- Markush non-hit visualization
Visualization of distinguishing structure parts
- ChemCurator
<http://www.chemaxon.com/wp-content/uploads/2014/05/ChemAxon-Patent-Curation.pdf>

US UGM 2014

Markush Session at ChemAxon US UGM, September 25-26, Cambridge, MA

We launch ChemCurator and overview existing Markush Editor, search and enumeration technologies

User presentations from Merck and Novartis, including (provisional)

- "Construction of a vast virtual library powered by ChemAxon's Markush Search Platform and its utility in molecular design - Zhengwei Peng, Merck & Co.
- The needs and challenges related to in-depth analysis of patent molecular spaces to support drug discovery projects. -Zhengwei Peng, Merck & Co.
- Placeholder topic: Markush search - Gregory Landrum, Novartis

Thank you for your attention

Tutorial

<http://www.chemaxon.com/library/markush-editor-6-3-version/>

User guide

<https://docs.chemaxon.com/display/markusheditor063/User%27s+Guide>

Download page

<http://www.chemaxon.com/download/markush-editor/>

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