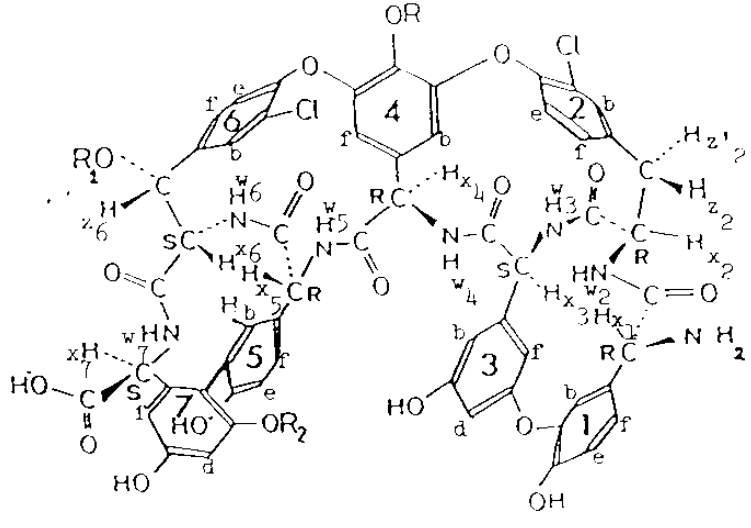
The International Conference for Science & Business Information 2009

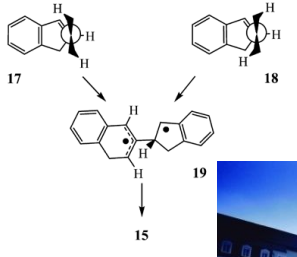
Chemical Depictions – The Grand Challenge in Patents



Dr. Marc Zimmermann

Image Extraction – an old Problem..?

- Short Overview on Chemical Structure Reconstruction
- CSR in Patents
  - Page Segmentation + Image Classification
  - Error Detection + Prediction
  - Markush Structures
  - Content Production Pipeline
- Conclusions



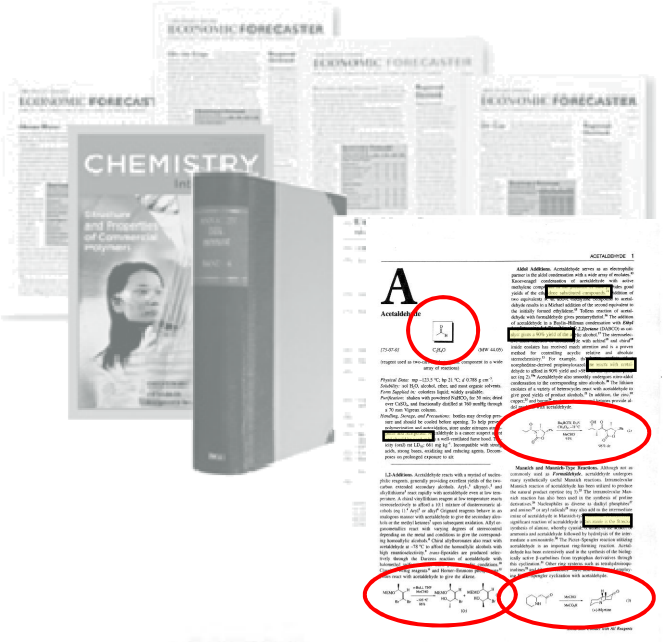
Archaeology

Chemistry / Pharmacology

Fraunhofer SCAI

Overview: Fraunhofer SCAI.Bio

- Information extraction in the life sciences
  - Biology
  - Chemistry
  - Medicine
  - Pharmacology
- Working on
  - Textual sources (PubMed, Journals)
  - Image sources (Journals, Thesis)
- Techniques
  - Dictionary based approaches (ProMiner)
  - Machine learning (Linda)
  - Expert systems (chemoCR)



Fraunhofer SCAI

Image Reconstruction is a famous Problem

- **Kekulé: OCR-optical chemical (structure) recognition,** R. McDaniel and Jason R. Balmuth. J. Chem. Inf. Comput. Sci., 32(4):373–378, 1992.
- **Chemical Literature Data Extraction: The CLiDE Project,** P. Ibison, M. Jacquot, F. Kam, A. G. Neville, R.W. Simpson, C. Tonnelier, T. Venczel and A.P. Johnson, J. Chem. Inf. Comput. Sci., vol. 33(3): 338-344, 1993.
- **Apparatus and method for optical recognition of chemical graphics**, R. Casey, S. Boyer, B. Oudot and K. Zilles, US Patent 5157736, 1992. **OROCS**
- **Optical recognition of chemical graphics,** S. Boyer, Document Analysis and Recognition, Proceedings of the Second International Conference on Document Analysis, 627–631, 20-22 Oct 1993.

But what happened to them?

New Initiatives

- **Optical structure recognition software to recover chemical information: OSRA,** V.I. Filippov and C.M. Nicklaus, J. Chem. Inf. Comput. Sci., 39(3):740-743, 2009.
- **CLiDE Pro: The latest generation of CLiDE,** T.A. Valko and P.A. Johnson, J. Chem. Inf. Comput. Sci., 49(4):780-787, 2009.
- **Automated extraction of chemical structure information from digital raster images,** J. Park, R.G. Rosania, A.K. Shedden, M. Nguyen, N. Lyu and K. Saitou, Chemistry Central Journal, 3:1-16, 2009. **ChemReader**
- **Machine learning and expert knowledge based evaluation of the chemoCR reconstruction result,** O. Domanova, Master Thesis, Bonn-Aachen International Center for Information Technology, University Bonn, 2009.

„Advanced Patent Search“

- Keywords (full text, title, abstract, claims)
- Publication / Application Number
- Applicant(s) / Inventor(s)
- Classification (ECLA, IPC)
- Date (filing, issue)

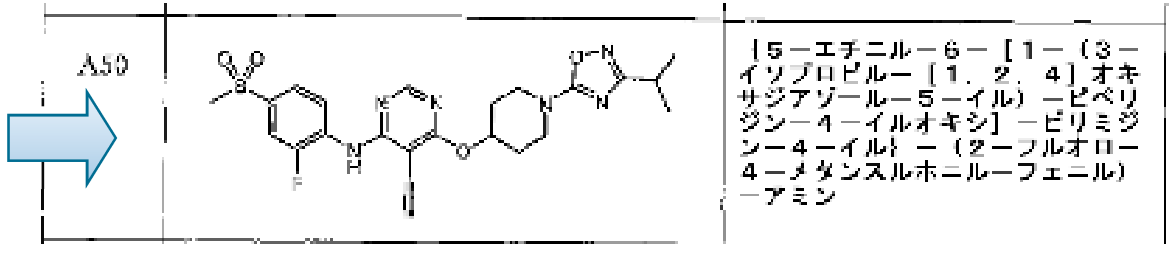
- WIPO
- USPTO
- EPO
- GOOGLE Patent Search

Advanced Searching from the Perspective of a Chemist

What is really interesting is – find me documents containing...

- similar structures
- structures containing a polycyclic aromatic ring system
- structures fulfilling my pharmacophore
- core structure in Asian patents
- a synthesis protocol
- biological target information
- …

graphical represented structure information



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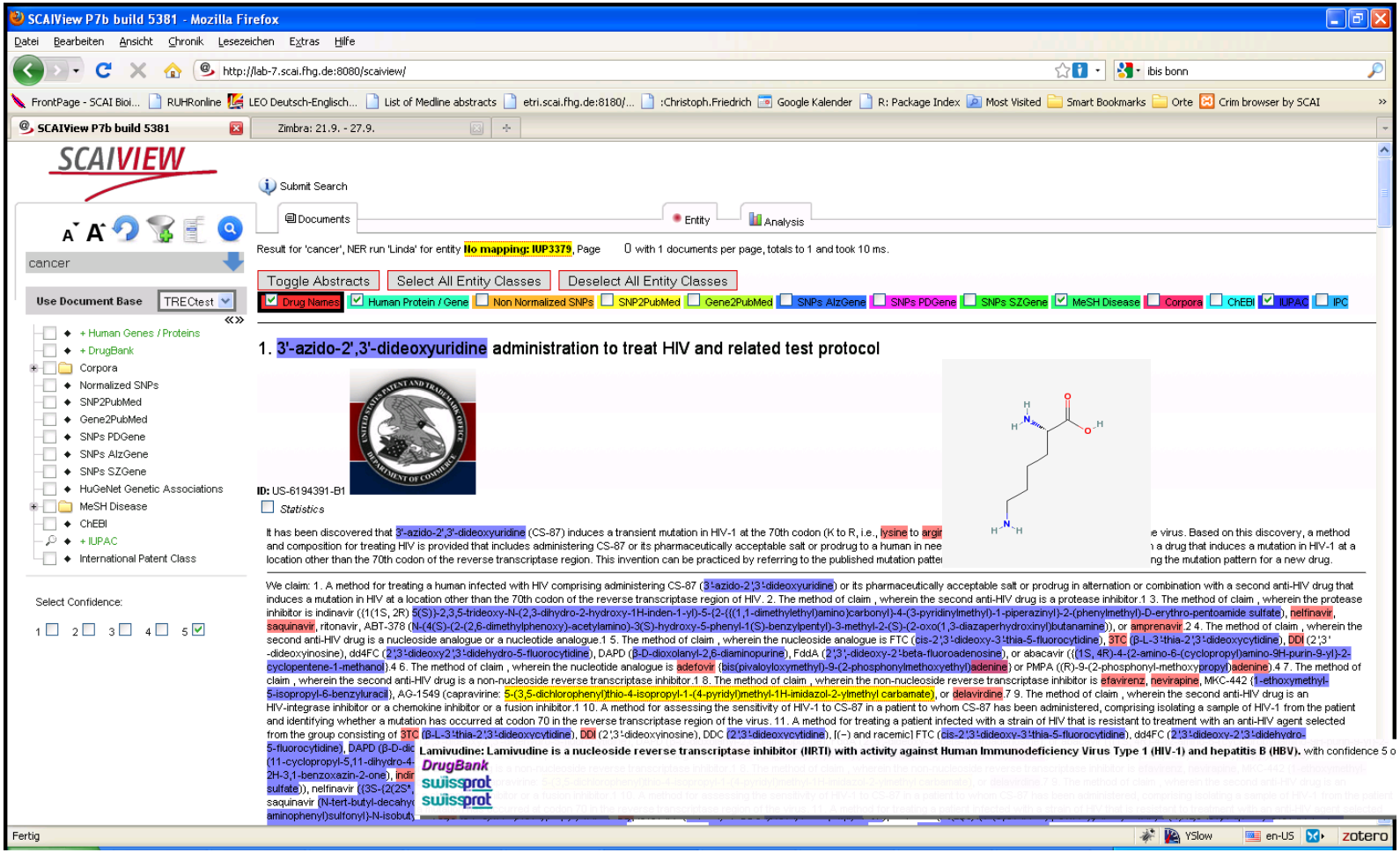
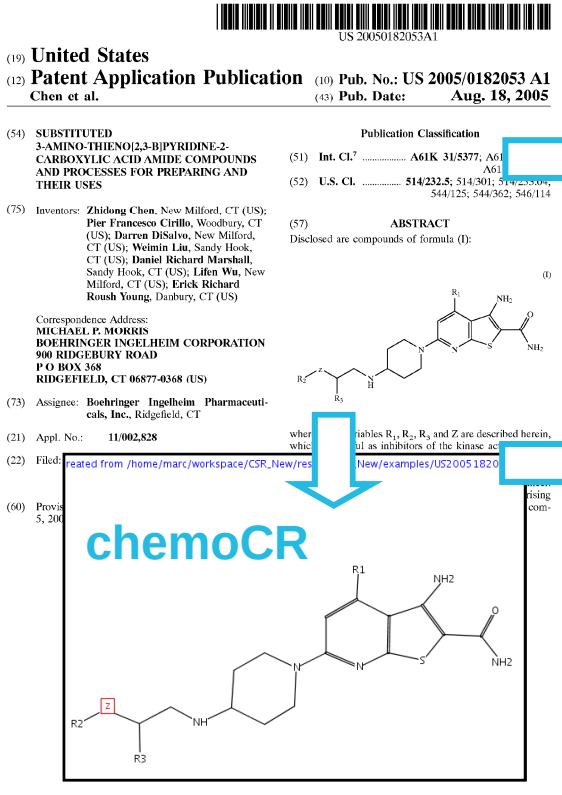
Idea: SCAIView Patent Retrieval



Goal: Multi-modal Information Extraction



US 20050182053A1

(19) United States

(12) Patent Application Publication (10) Pub. No.: US 2005/0182053 A1

Chen et al. (43) Pub. Date: Aug. 18, 2005

(54) SUBSTITUTED 3-AMINO-THIENO[2,3-B]PYRIDINE-2-CARBOXYLIC ACID AMIDE COMPOUNDS AND PROCESSES FOR PREPARING AND THEIR USES

(75) Inventors: Zhidong Chen, New Milford, CT (US); Pier Francesco Cirillo, Woodbury, CT (US); Darren DiSalvo, New Milford, CT (US); Weimin Liu, Sandy Hook, CT (US); Daniel Richard Marshall, Sandy Hook, CT (US); Lifen Wu, New Milford, CT (US); Erick Richard Roush Young, Danbury, CT (US)

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(73) Assignee: Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT

(21) Appl. No.: 11/002,828

(22) Filed:

(60) Provis 5, 200

Publication Classification

(51) Int. Cl.[7] A61K 31/5377; A61 A61

(52) U.S. Cl. 514/232.5; 514/301; 514/253.04; 544/125; 544/362; 546/114

(57) ABSTRACT

Disclosed are compounds of formula (I):

(I)

wher iables R_1, R_2, R_3 and Z are described herein, whic ul as inhibitors of the kinase ac

rising com-

created from /home/marc/workspace/CSR_New/res New/examples/US20051820

chemoCR

ProMiner (NER)

Patent Space Index

SCAIView

3-AMINO-THIENO[2,3-BIPYRIDINE-2-CARBOXYLIC ACID AMIE
PROCESSES FOR PREPARING AND THEIR USES

RELATED APPLICATIONS

[0001] This application claims priority to U.S. prov application No. 601527,522 filed on Dec. 5, 2003. application is also related to U.S. patent applicati Nos. 101453,175 and 101730,172.

TECHNICAL FIELD OF THE INVENTION

[0002] This invention relates to substituted 3-amin thieno[2,3-b]pyridine-2-carboxylic acid amide com useful as inhibitors of the kinase activity of the IK (IKK) complex. The compounds are therefore use treatment of IKK-mediated diseases including autoimmune diseases, inflammatory diseases and cancer. The invention also relates to processes for preparing such compounds and pharmaceutical compositions comprising them

BACKGROUND OF THE INVENTION

[0003] NF-KB or nuclear factor KB is a transcription factor that induces the expression of a large number of pro-inflammatory and anti-apoptotic genes. These include cytokines such as IL-1, IL-2, TNF-a and IL-6, chemokines including IL-8 and RANTES, as well as other pro-inflammatory molecules including COX-2 and cell adhesion molecules such as ICAM-I, VCAM-I, and E-selectin. The NF-KB family includes homo- and heterodimeric transcription factors composed of members of the Re1 family (see for example P. A. Baeurle and D. Baltimore, Cell, 1996,87, 13). Under resting conditions, NF-KB is present in the cytosol of cells as a complex with IKB. The IKB family of proteins

proteins
protein families
protein complex
compound
process
drug class
disease
pathways

Chemical Page Segmentation and Image Classification

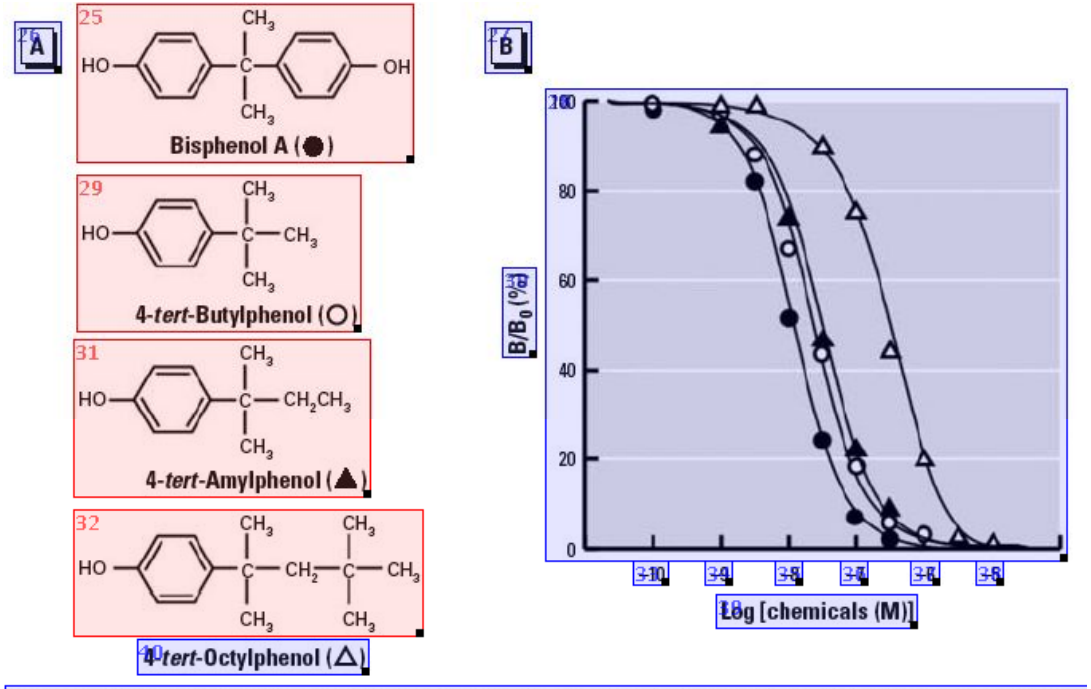

Figure 4. Chemical structure of BPA and its derivatives lacking the phenol group and their dose–response curves in the radioligand receptor binding assay for ERR-γ. (*A*) Chemical structure of BPA and its derivatives with the alkyl group at the position of phenol group: 4-*tert*-butylphenol (a methyl group); 4-*tert*-amylphenol (an ethyl group); and 4-*tert*-octylphenol (a *tert*-butyl methyl group). (*B*) Binding activities of BPA, 4-*tert*-butylphenol, 4-*tert*-amylphenol, and 4-*tert*-octylphenol examined by the competitive binding assay using [^{3}H]BPA and GST-ERR-γ–LBD; representative curves indicate the IC_{50} value closest to the mean IC_{50} from at least five independent assays for each compound.

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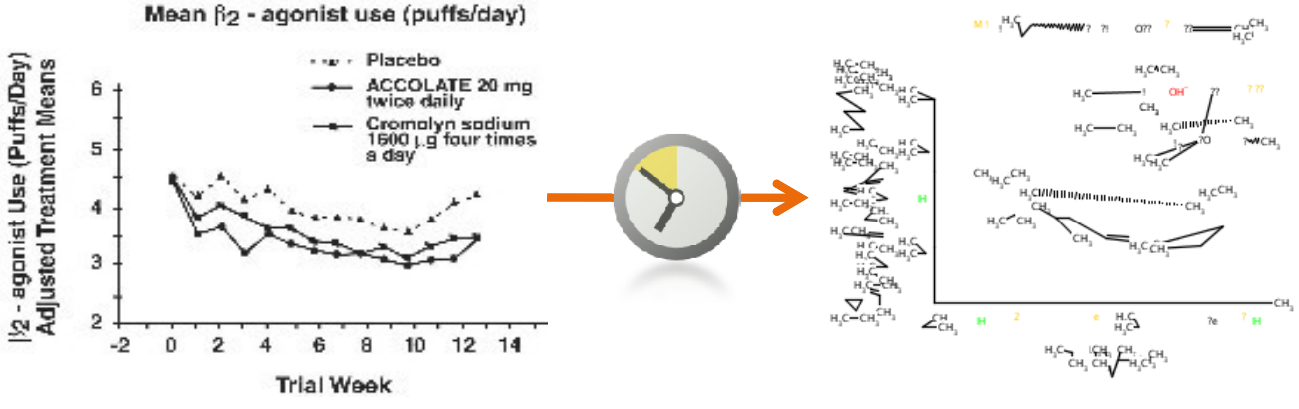
Motivation for Image Classification

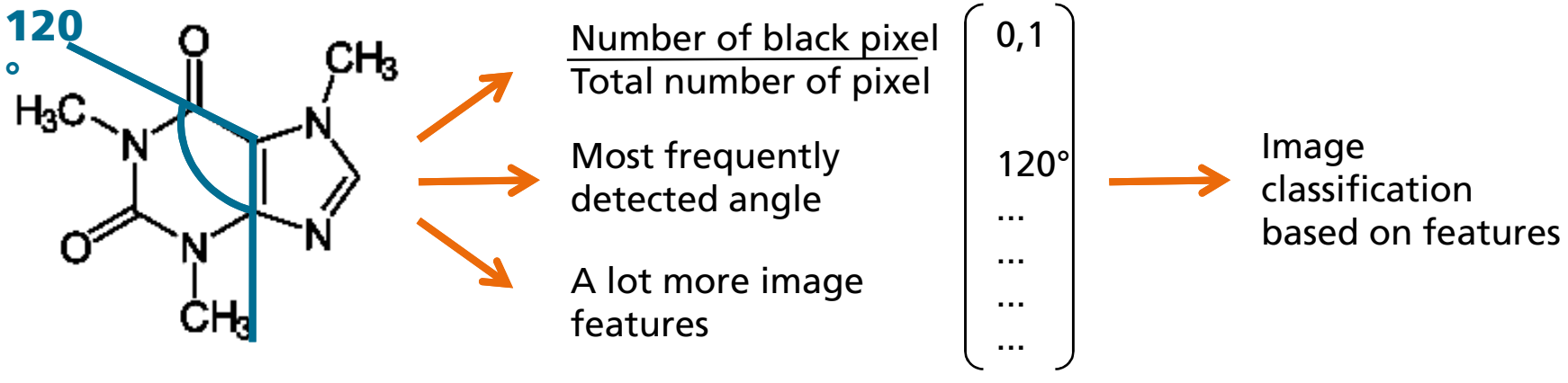
- Example for an image without chemical content and it´s reconstruction with chemoCR



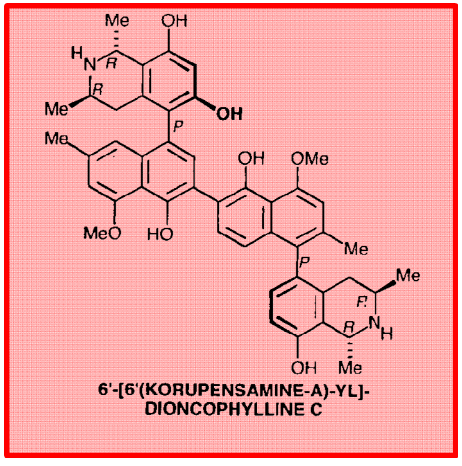
- Effective reconstruction of big image stacks
- Full page scans: classification of page segments

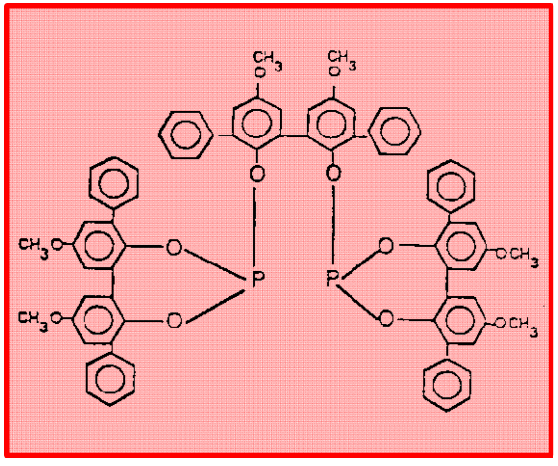
Concept of Image Classification

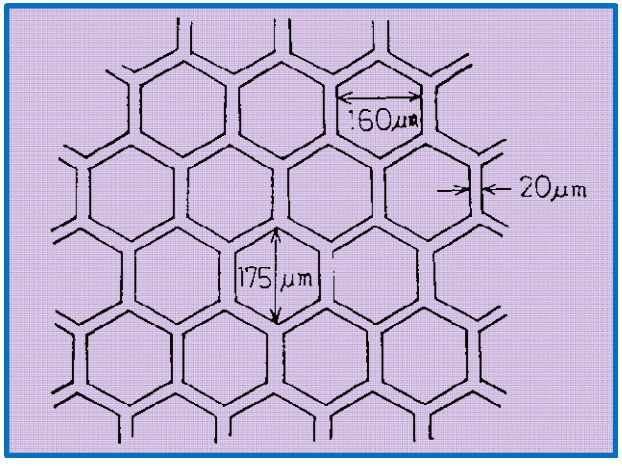
- Problem
  - No well defined rule, whether a image is a structural formula or not.
- Approach
  - Calculate comparable **image features** and use machine learning

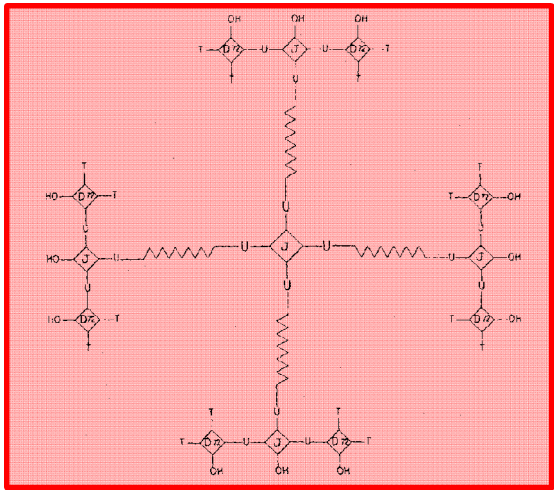


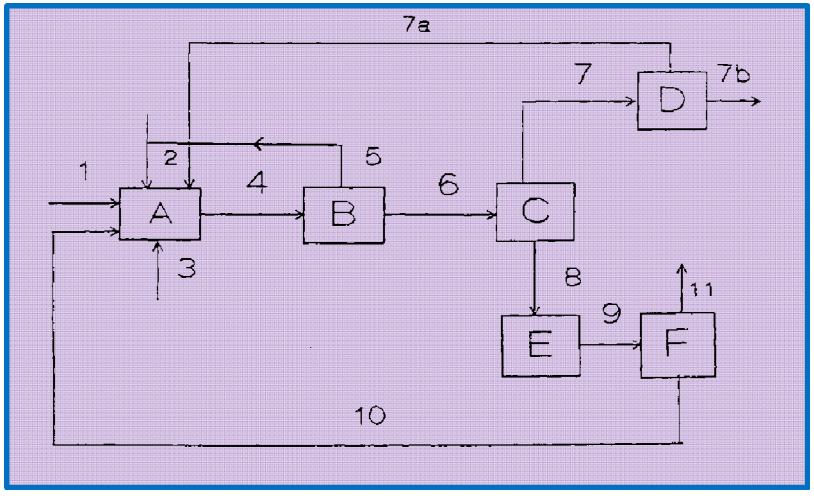
Some Examples from Patents (I)











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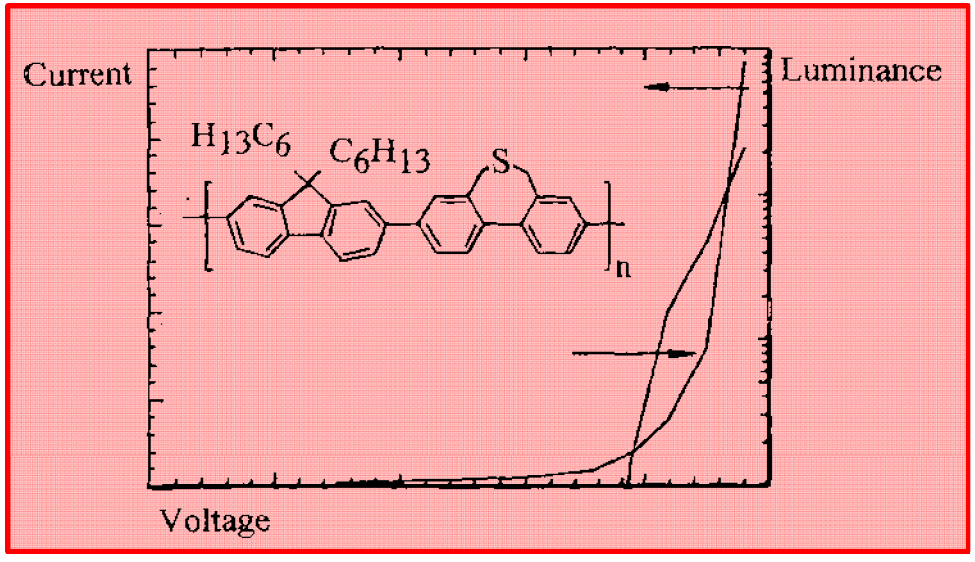
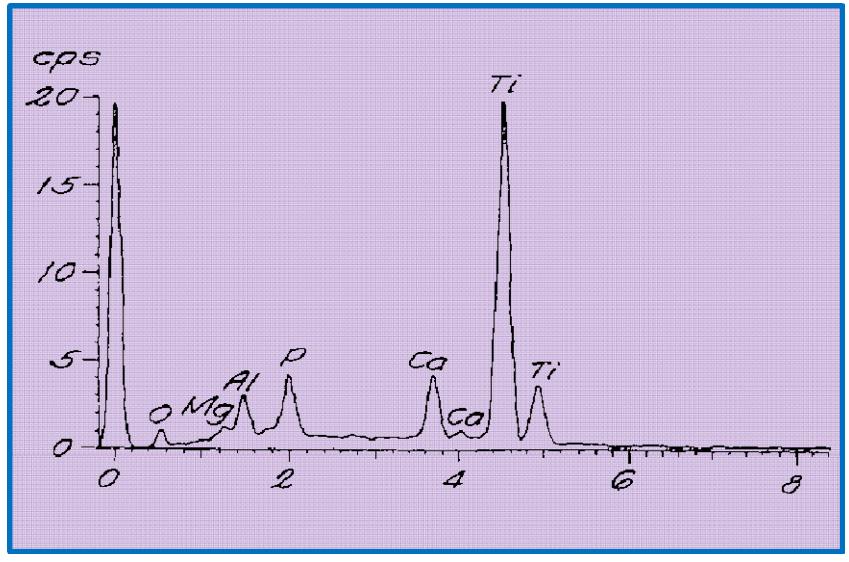
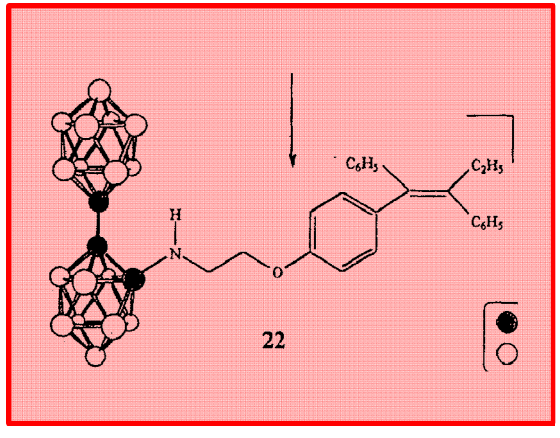
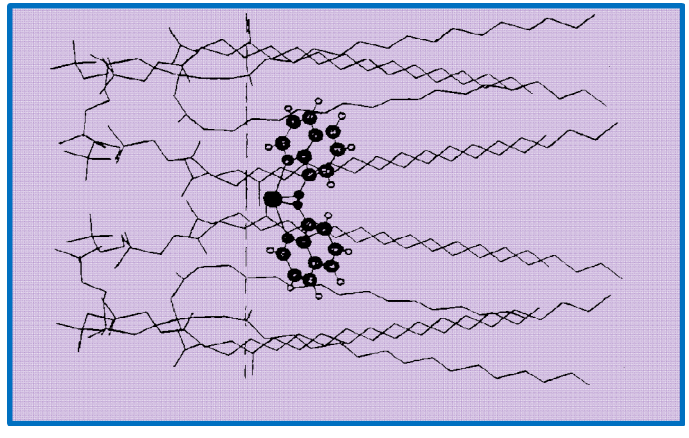
Some Examples from Patents (II)









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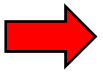
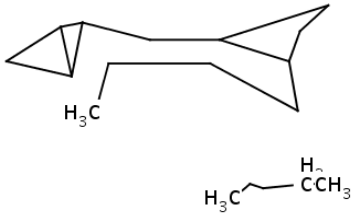
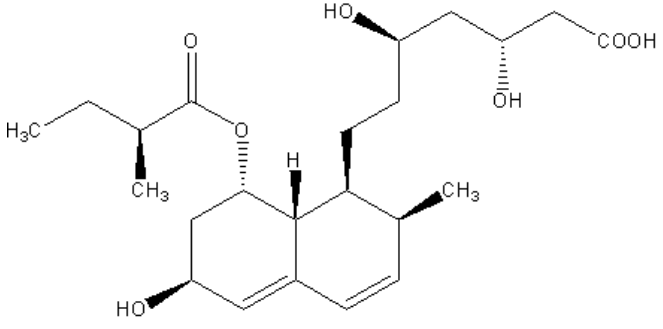
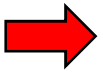
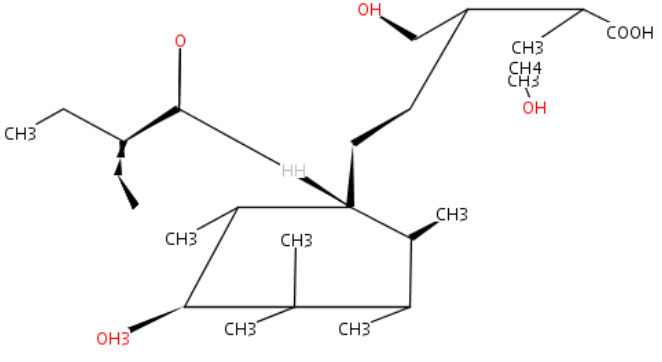
Beautiful Artwork But Wrong Molecule



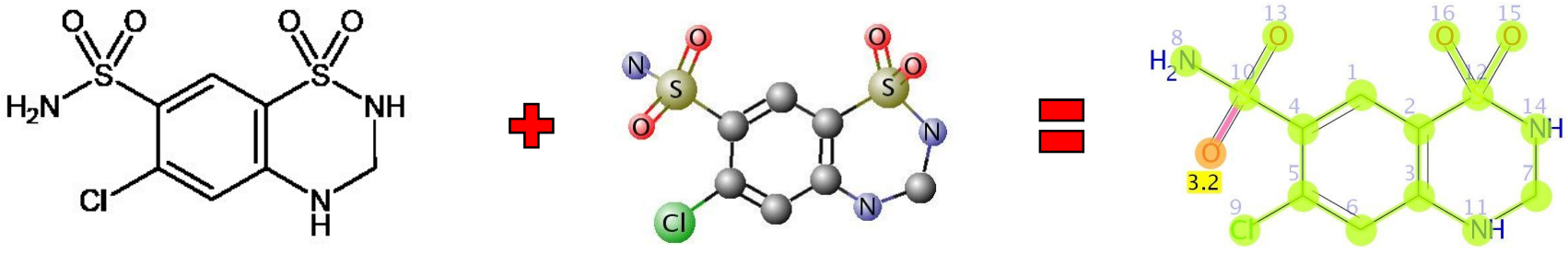








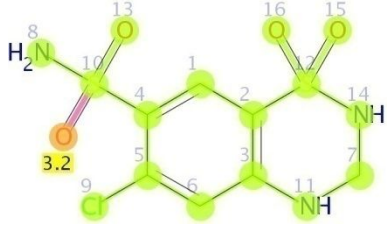
Quality Measure: Graph Matching



- SimilarityMCD (Minimal Chemical Distance)
  - Module from InfoChem
- Graph-matching on
  - Reconstruction result of chemoCR
  - The reference molecule
- Results in
  - Numerical value, [0,1]

Automatic Assessment of the Reconstruction Quality

- SimilarityMCD in [0,1]
  - 1.0 – fully correct reconstruction
- Threshold



SimilarityMCD = 0.95

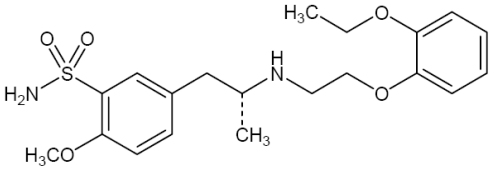
≥ **Correct** → Database, Analysis, Virtual Screening,…

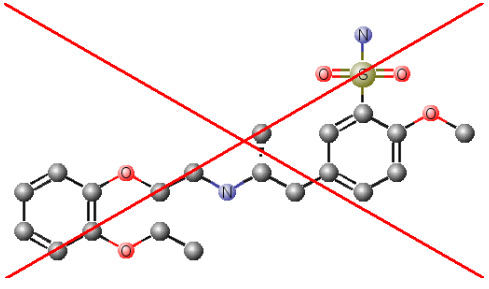
< **Wrong** → Manual post processing by an expert

- Aim
  - Minimize false positive rate

Challenge

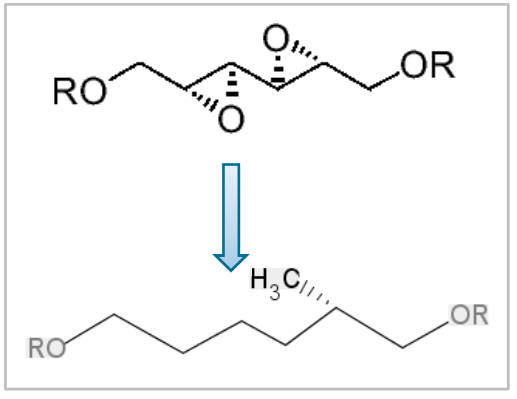
- Problem
  - Predict the quality of the reconstruction result without a reference molecule
- Solution
  - Machine learning
- Expected results
  - Quality of new reconstructions estimated by trained models



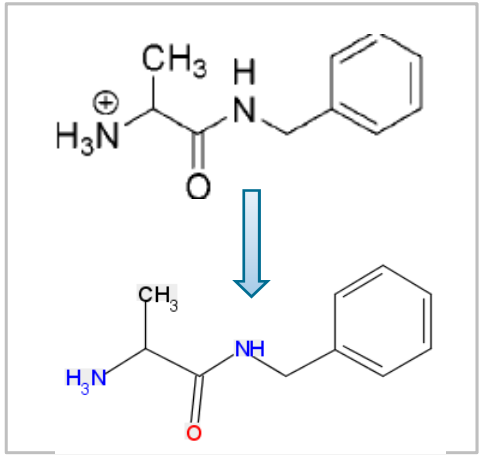


Chemical Error Classification System

- MISSED
  - BOND_MISSED
    - COMPLETE_BOND_MISSED
    - ORDER_BOND_MISSED
    - **CHIRAL_BOND_MISSED**



  - SYMBOL_MISSED
    - ATOM_SYMBOL_MISSED
    - ISOTOPE_SYMBOL_MISSED
    - **CHARGE_SYMBOL_MISSED**
    - RADICAL_SYMBOL_MISSED



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Chemical Error Classification System

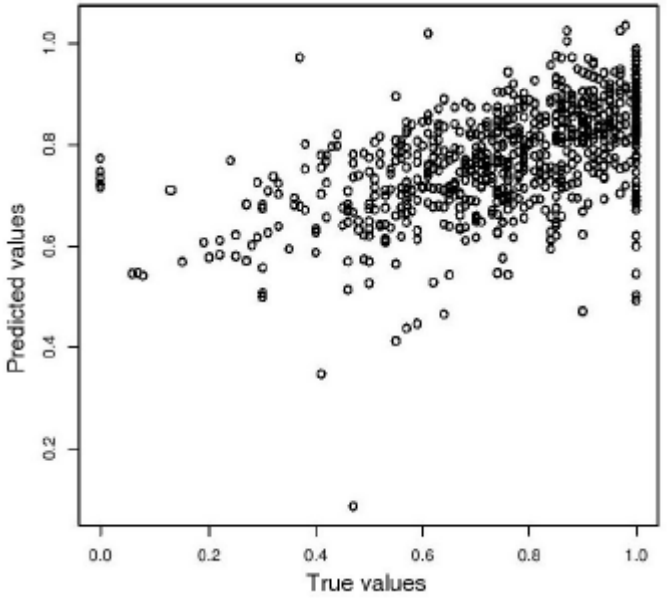
- Assigned based on comparison of
  - Result of the reconstruction
  - Reference molecule
- Hierarchical system
- 4 super classes
  - AS_STRUCTURE
  - ERROR
  - MISSED
  - ADDED

1. _AS_STRUCTURE
   a) GRAPHIC_AS_STRUCTURE
   b) TEXT_AS_STRUCTURE
      i. CHAR_TEXT_AS_STRUCTURE
      ii. NUMBER_TEXT_AS_STRUCTURE
   c) ARROW_AS_STRUCTURE
      i. ELECTRON_ARROW_AS_STRUCTURE
      ii. REACTION_ARROW_AS_STRUCTURE
   d) BRACKET_AS_STRUCTURE
      i. POLYMER_BRACKET_AS_STRUCTURE
      ii. REACTION_BRACKET_AS_STRUCTURE
   e) NEWMAN_AS_STRUCTURE
   f) CHARGE_AS_STRUCTURE
2. _ERROR
   a) KEKULE_RING_ERROR
   b) BOND_ERROR
      i. COORD_BOND_ERROR
      ii. H_BOND_ERROR
      iii. WAVY_BOND_ERROR
      iv. CROSS_BOND_ERROR

Some preliminary Results

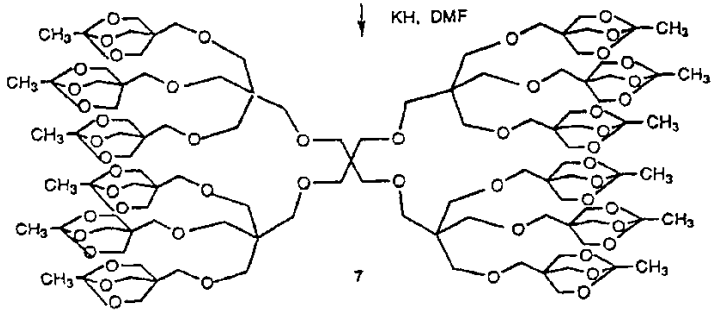
Performance measure	Training data	Test data
MSE *)	2.466×10^{-2}	2.976×10^{-2}
Correlation coefficient	5.816×10^{-1}	5.393×10^{-1}

*) mean squared error

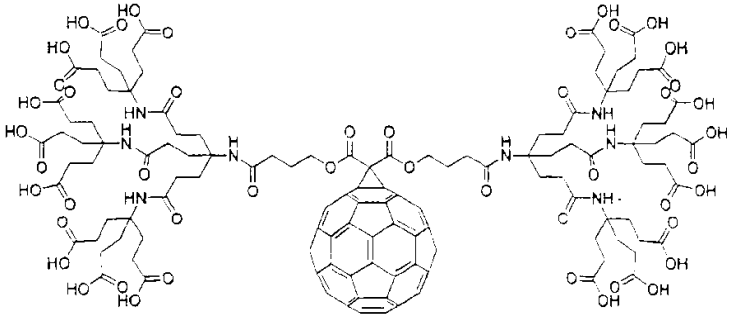


Category: Complex Molecules (I)

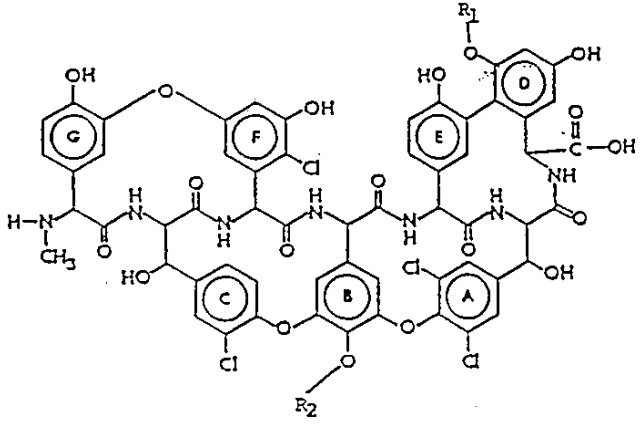
EP 0751952 B1: Displacement Chromatography of Proteins



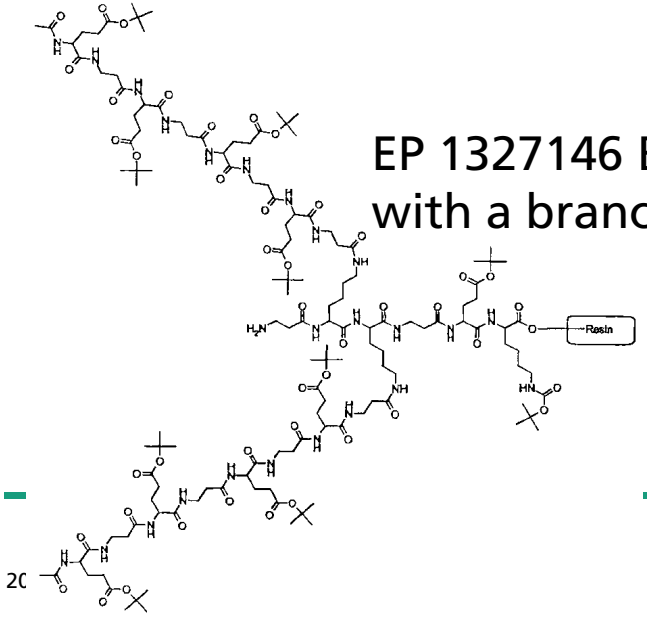
EP 1056475 B1: Dendrimere Fullerene derivate



EP 0211490 B1: Antibiotics of the Vancomycin-Class



EP 1327146 B1: Compounds with a branched Linker



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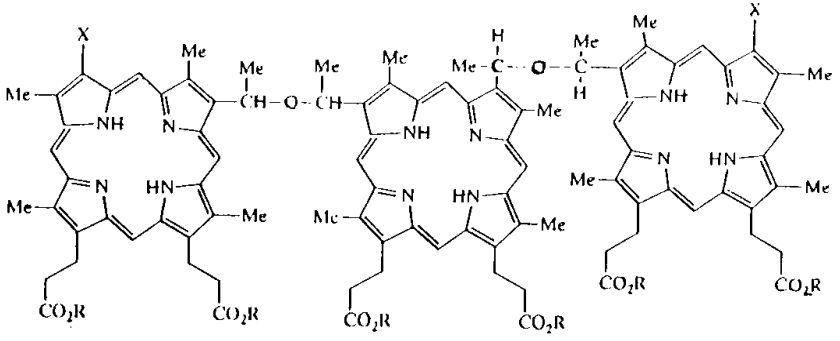
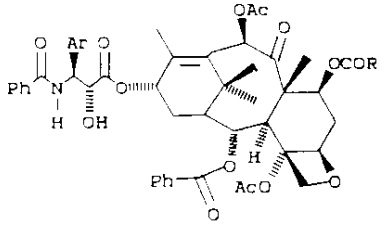
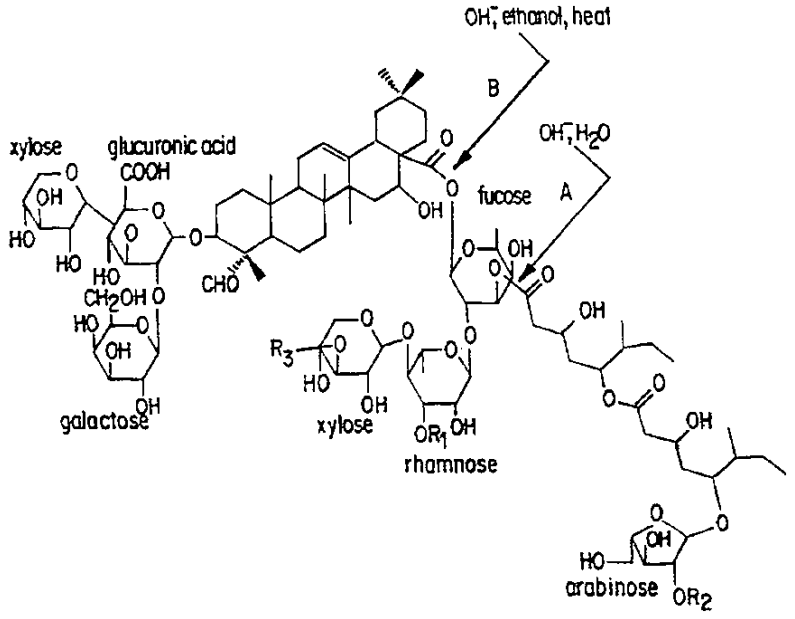
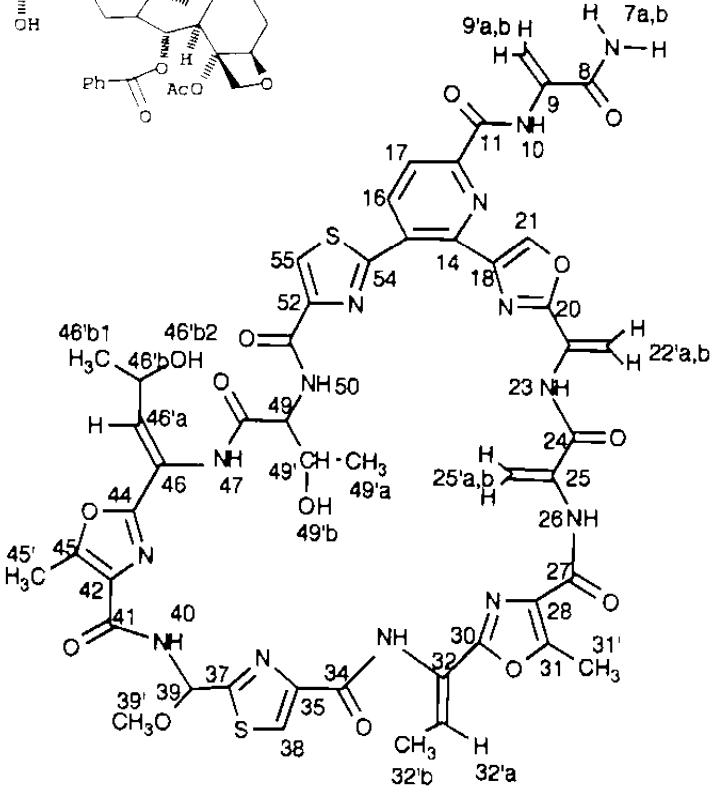
Category: Complex Molecules (II)





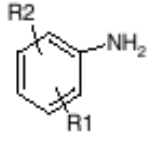




Why is Markush famous?

- Dr. Eugene A. Markush (1887-1968)
- Founder of Pharma Chemical Corporation Bayonne, NJ in 1917
- Did not(!) invent generic structures
- Patent for method of preparing a generic group of pyrazalone dyes for wool or silk

The process for the manufacture of dyes which comprised coupling with a halogen-substituted pyrazolone, a diazotized unsulphonated material prepared from a compound having the formula



wherein R1 and R2 are independently selected from the

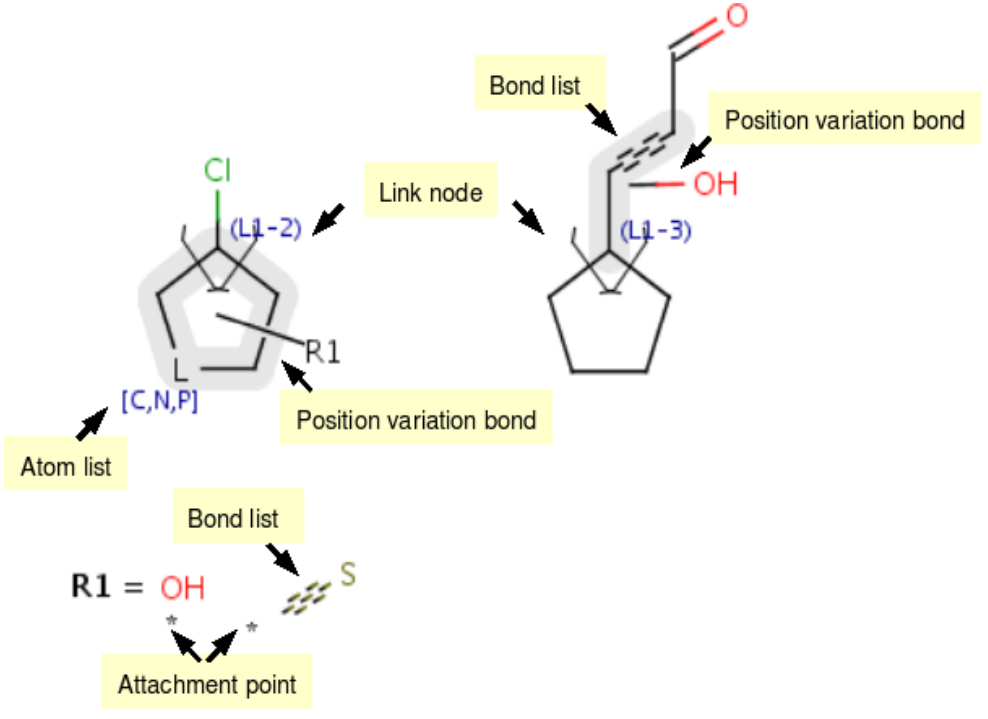
First claim of patent US 1506316

- The claim was challenged as being too unspecific
- Granted in 1924 by the US commissioner of Patents

Fraunhofer SCAI

Markush Structures in Principle

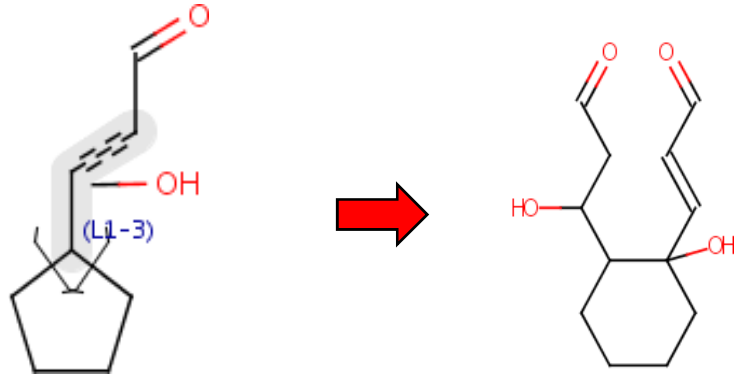
- No general definition
- Core structure
  - Multiple elements
  - Nested elements
- Additional information
  - R-group definition



Markush Structure Analysis

Core Structure

- Nested elements → Order?
- Link node most powerful
- Creates just valid structures



Additional Information

- Structure list
- Formal string
- Structured text
- Natural language

Structured text → E is selected from the group consisting of CR^9R^9, CR^9, O, N and NH;

Formal strings → G is CH or N;

J is CR_9R_9, CR_9, C=O, C=S, or N;

Natural language → the dashed line represents an optional double bond, provided that J is not C=O, C=S or CR_9R_9 when a double bond is present;

Y is $-NR_3$, O or S;

Structured text → n_2 and n_3 are each independently 0-2;

n_4 is 0-3;

Fraunhofer SCAI

Textual Annotations

A, B and D are each independently selected to be CR_{4b} or N, provided that at least one A, B or D is N;

E is selected from the group consisting of CR^9R^9, CR^9, O, N and NH;

G is CH or N;

J is CR_9R_9, CR_9, C=O, C=S, or N;

the dashed line represents an optional double bond, provided that J is not C=O, C=S or CR_9R_9 when a double bond is present;

Y is $-NR_3$, O or S;

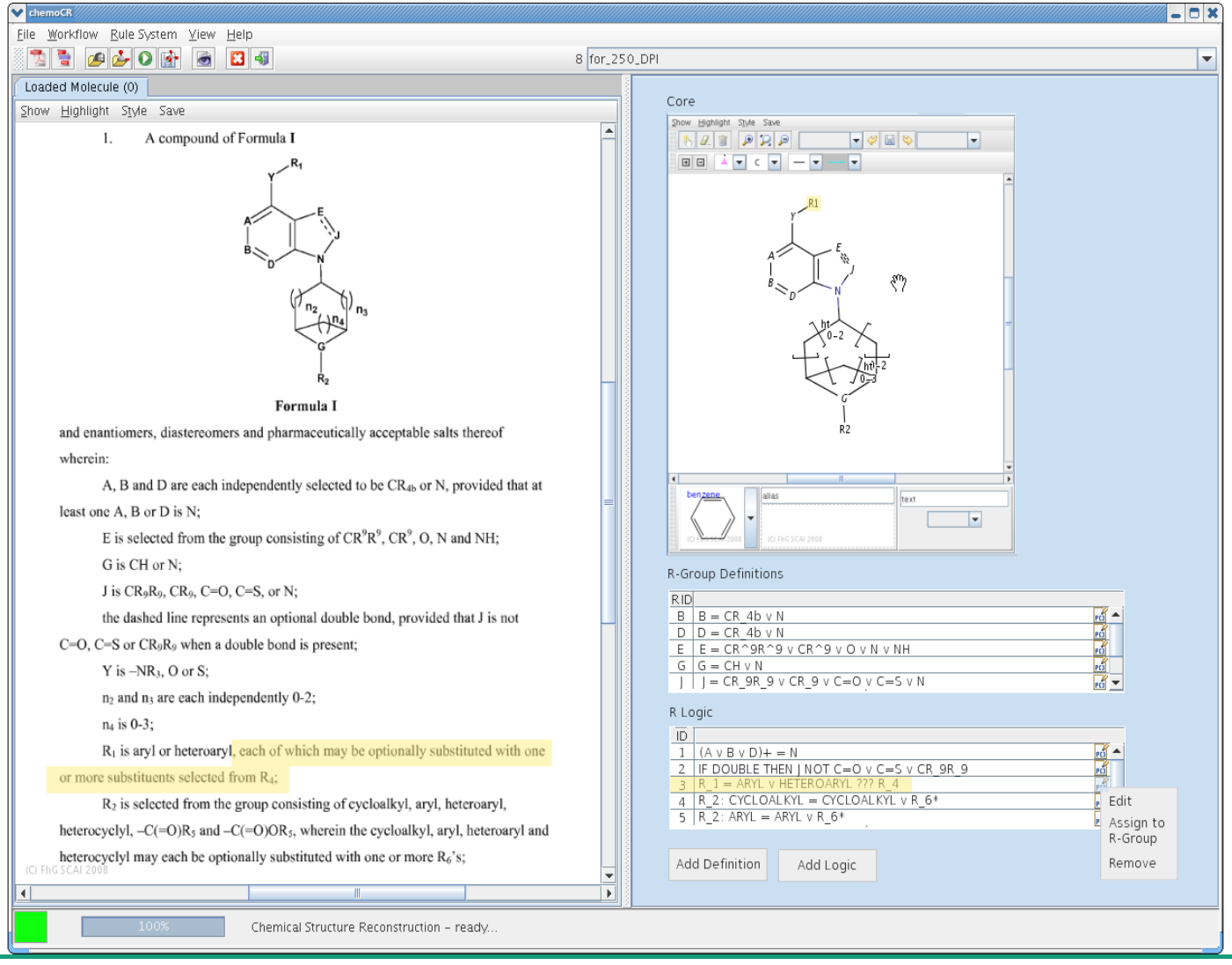
n_2 and n_3 are each independently 0-2;

n_4 is 0-3;

R_1 is aryl or heteroaryl, each of which may be optionally substituted with one or more substituents selected from R_4;

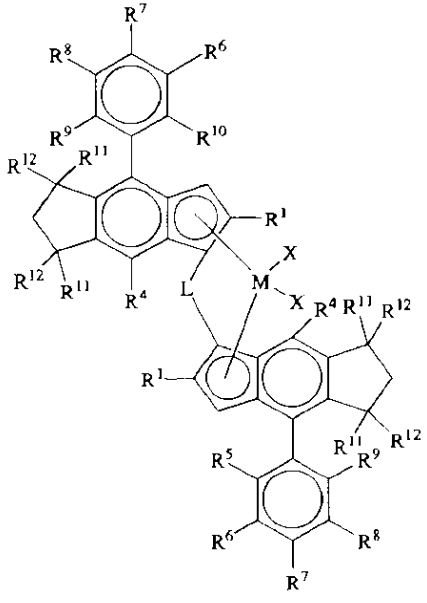
R-group
Chem. Element
Relation

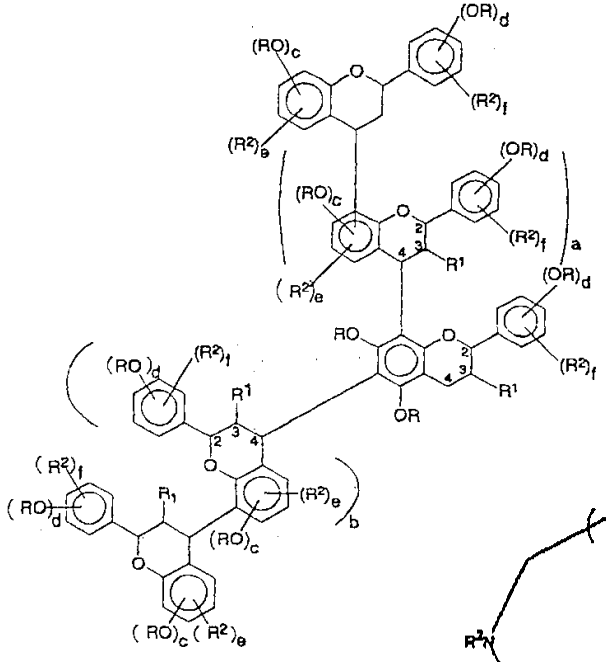
Wanted: an Editor

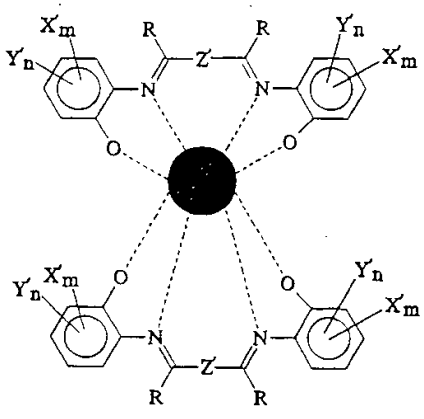


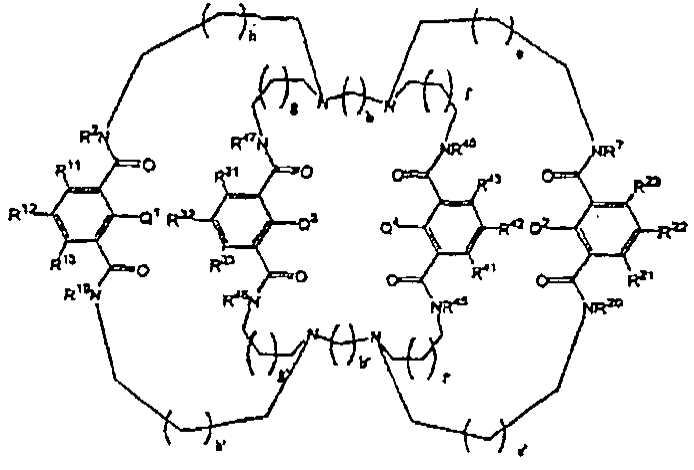
Fraunhofer SCAI

Some Examples from Patents (I)

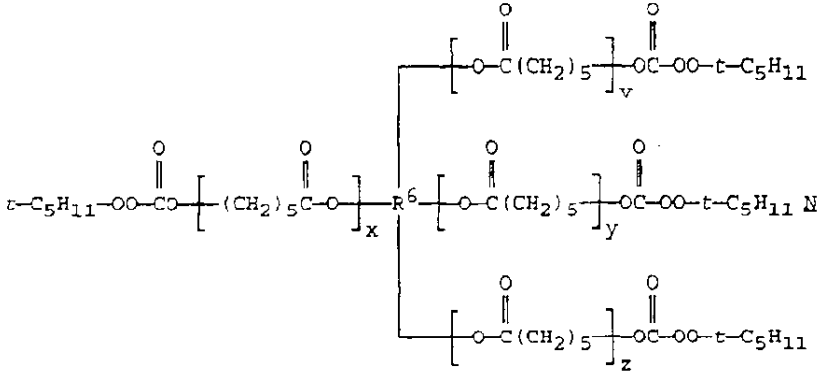


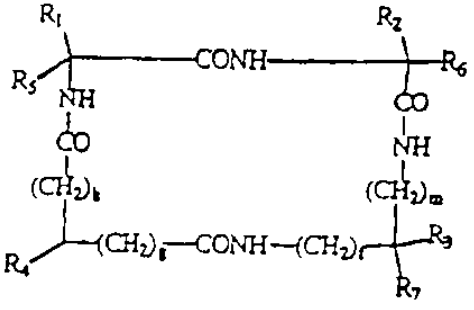


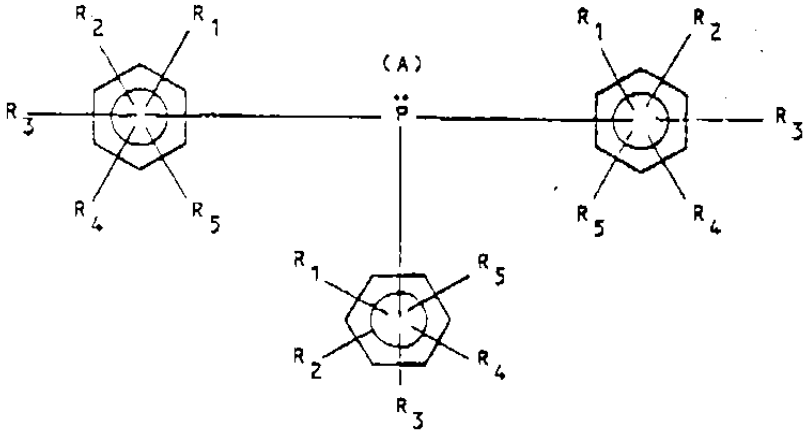


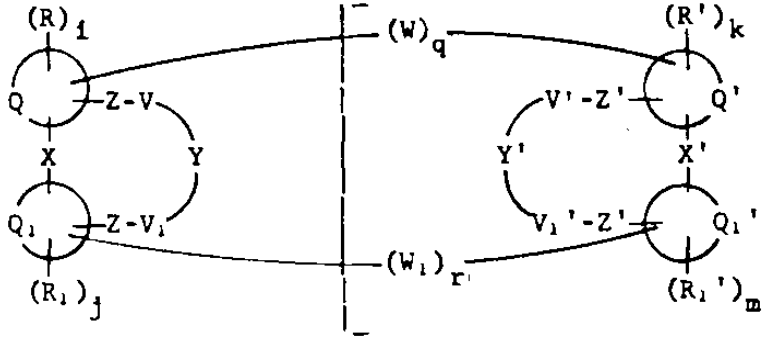


Some Examples from Patents (II)



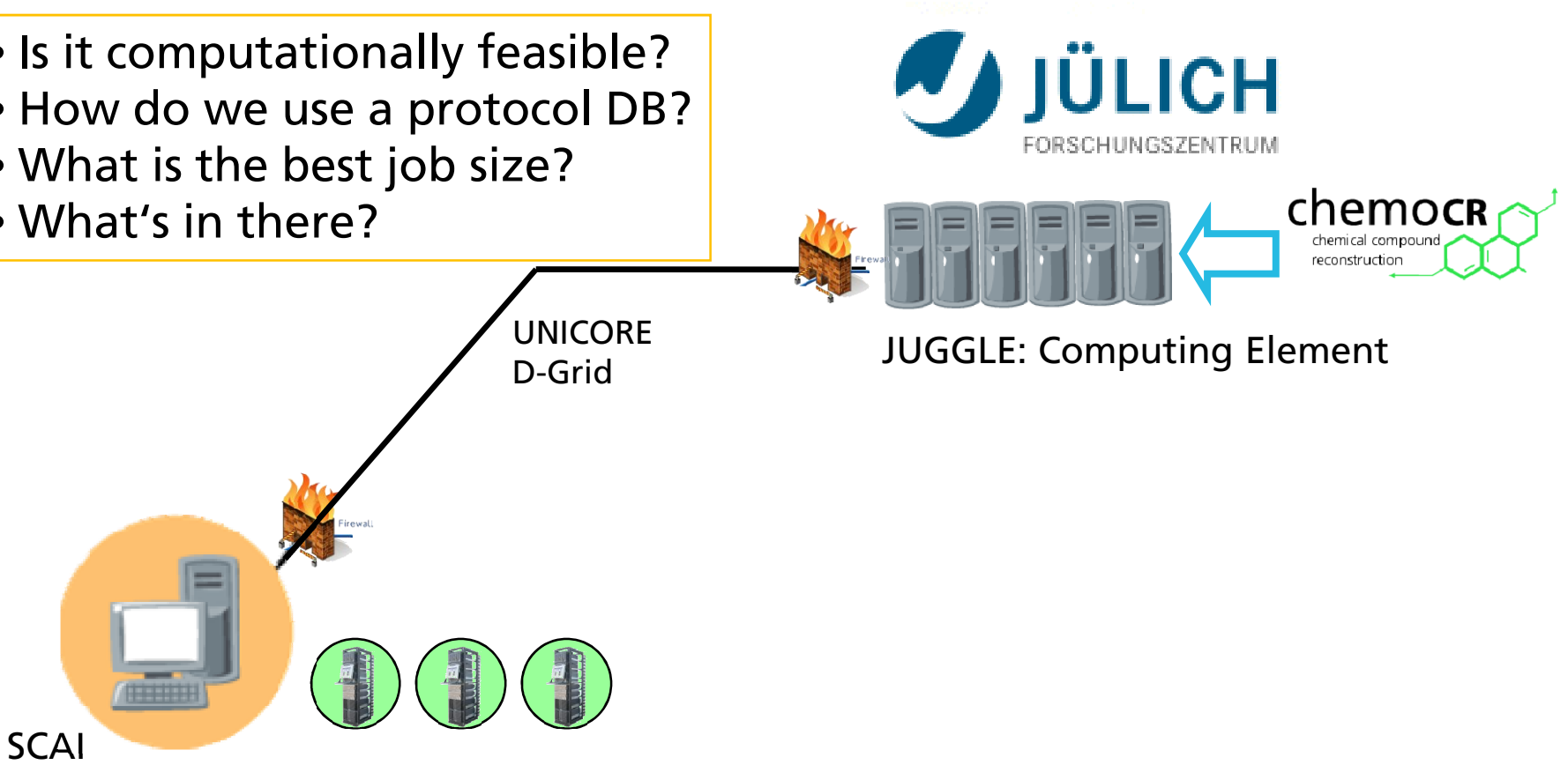






The Grand Patent Challenge: Content Production

- Is it computationally feasible?
- How do we use a protocol DB?
- What is the best job size?
- What's in there?

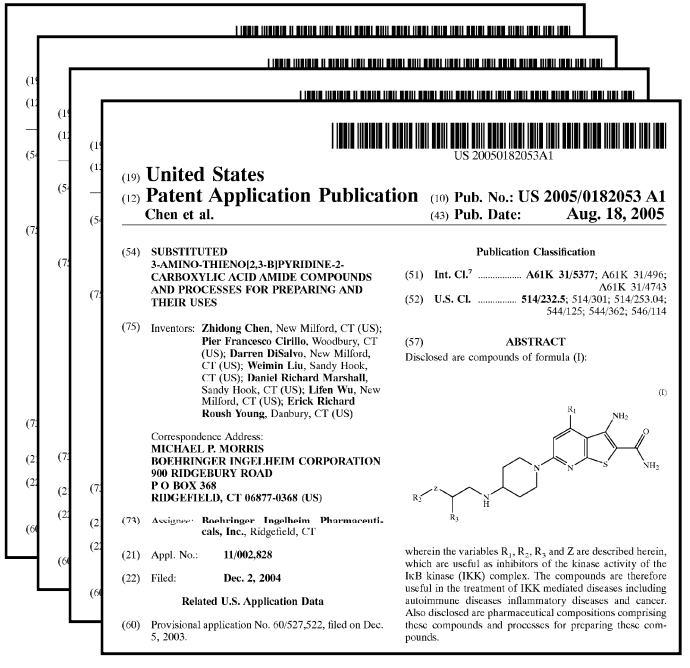


- Storage Element: Input (200Gb) and Output
- License Server
- ProtocolDB

Job Definition in the Grid

What is the optimal job size?

- Load balancing
- Context
- Dependencies
- Queuing mechanism
- Job management
- Failures
- Overhead



US 20050182053A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2005/0182053 A1**

Chen et al. (43) **Pub. Date: Aug. 18, 2005**

(54) **SUBSTITUTED 3-AMINO-THIENO[2,3-B]PYRIDINE-2-CARBOXYLIC ACID AMIDE COMPOUNDS AND PROCESSES FOR PREPARING AND THEIR USES**

(75) Inventors: **Zhidong Chen**, New Milford, CT (US); **Pier Francesco Cirillo**, Woodbury, CT (US); **Darren DiSalvo**, New Milford, CT (US); **Weimin Liu**, Sandy Hook, CT (US); **Daniel Richard Marshall**, Sandy Hook, CT (US); **Lifen Wu**, New Milford, CT (US); **Erick Richard Roush Young**, Danbury, CT (US)

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(21) Appl. No.: **11/002,828**

(22) Filed: **Dec. 2, 2004**

Related U.S. Application Data

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(52) **U.S. Cl.** **514/232.5**; 514/301; 514/253.04; 544/125; 544/362; 546/114

(57) **ABSTRACT**

Disclosed are compounds of formula (I):

(I)

wherein the variables R_1, R_2, R_3 and Z are described herein, which are useful as inhibitors of the kinase activity of the IκB kinase (IKK) complex. The compounds are therefore useful in the treatment of IKK mediated diseases including autoimmune diseases inflammatory diseases and cancer. Also disclosed are pharmaceutical compositions comprising these compounds and processes for preparing these compounds.

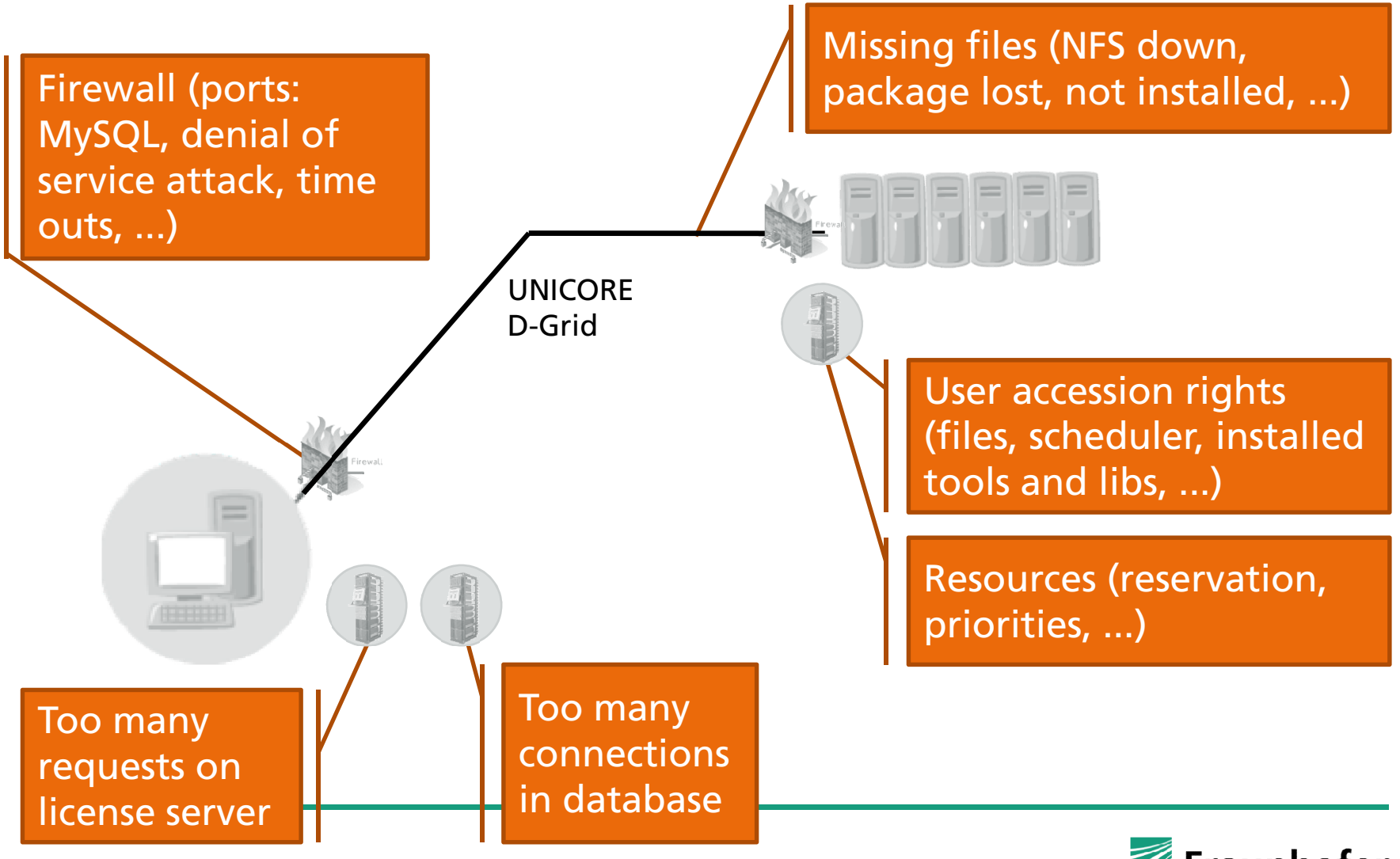
Different Scheduling Strategies

- Let us assume:
  - We process 25,000 documents
  - A document has on average 20 pages
  - A page contains on average 10 molecules

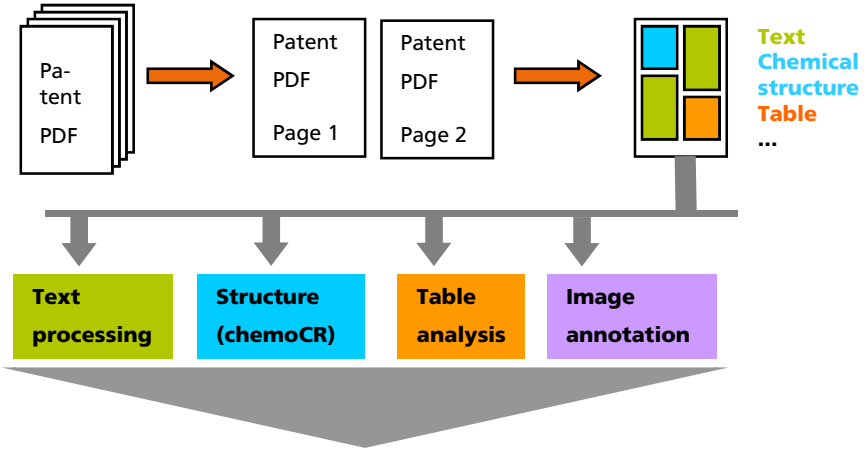
	Per Document	Per Page	Per Chemistry
Number of Jobs	25,000	500,000	5,000,000
Run Time (sec.)	2400	120	12

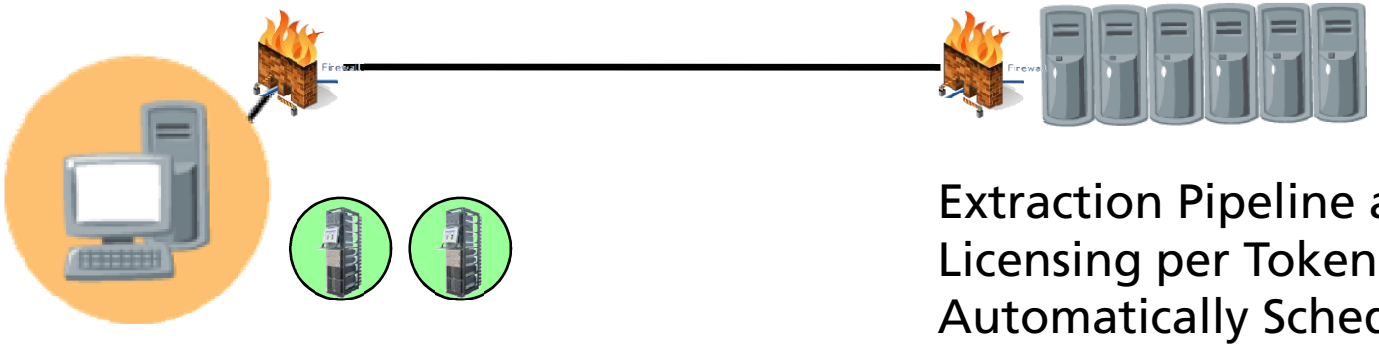
Where do we achieve the best crunching factor?

Technical Issues and Pitfalls



Outlook: Next Generation?





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Licensing per Tokens
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Fraunhofer SCAI

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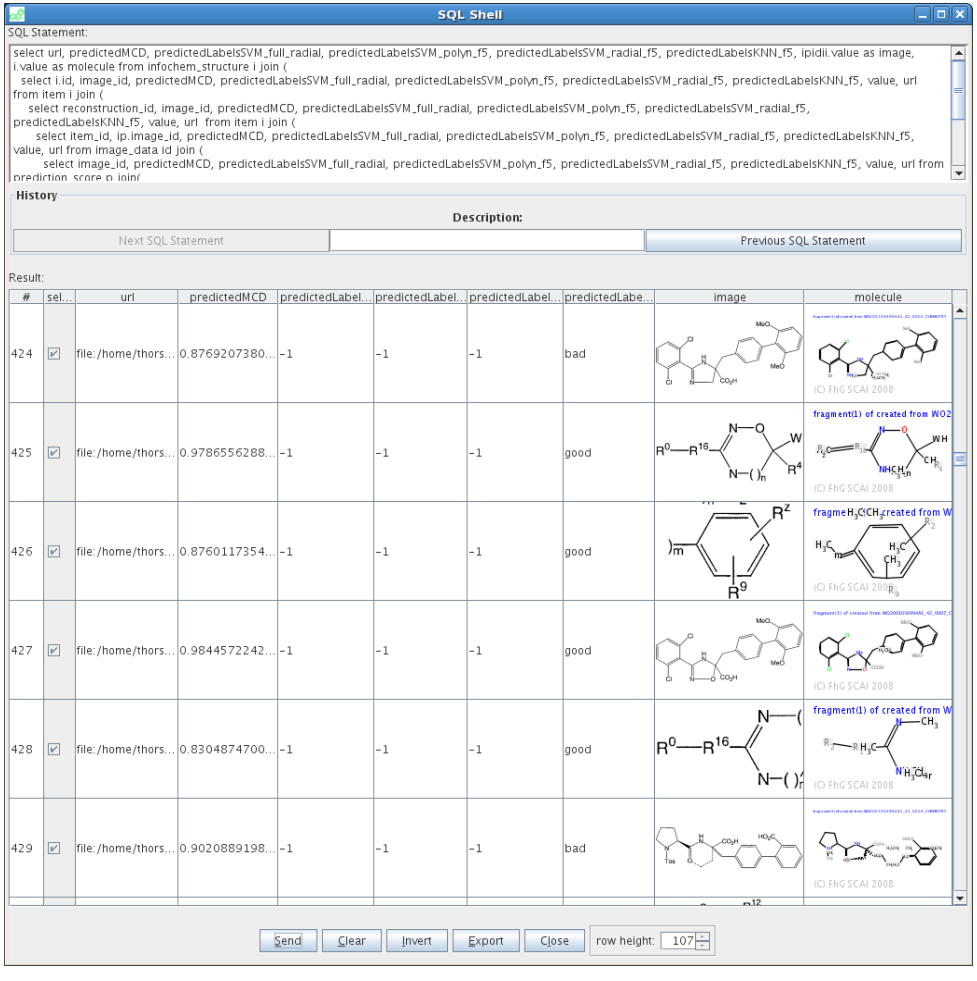
Images	Total	AVG.
Documents	23,945	
Run Time (h)	45,360	0.1
Pages	692,576	28.9
Structures	531,505	22.2
Max page	946	
Data (Gb)	100.9	

Full Text	Total Docs	AVG.
Genes/ Proteins	824,415	30.27
IUPAC	128,997	2.39
Drug	170,857	45.66



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IPC Class/At least one Entity mention	Number of Patents
A61 Medical Science	34,704
C12 Enzyme Technology	4,851
A61 + C12	35,381
Gene/Protein	43,103
ATC Class	52,552
MeSH Disease	38,474
MedDRA	55,748
Drug Name	44,001
IUPAC	52,720

Example of IUPAC Annotation

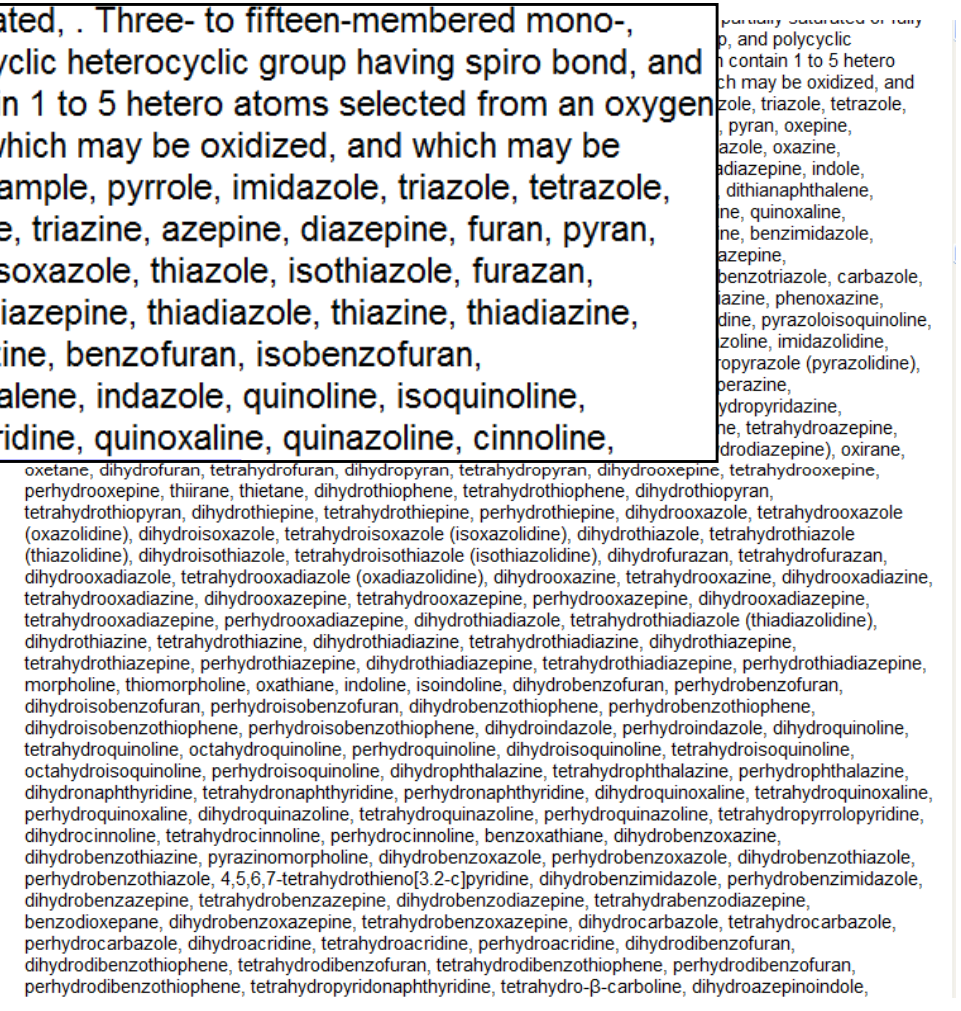
tetrahydrodiazepine and diazepane. The compound according to claim 1, wherein ring B is a ring selected from pyrrole, imidazole, pyrazole, thiazole, oxazole, pyridine, pyrimidine, dihydrotriazine, pyrazine and dihydropyrimidine. The compound according to claim 1, wherein the compound of formula (I) is 5,6,7,8-tetrahydropyrimido[4,5-d]pyrimidine-2-carbonitrile, pyrazolo[1,5-a]pyrimidine-5-carbonitrile, 2,3-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, pyrazolo[1,5-a][1,3,5]triazine-2-carbonitrile, 1H-pyrimido[4,5-e][1,3,4]oxadiazine-7-carbonitrile, 1H-pyrazolo[3,4-

group which may have a substituent(s).1C 3 2 1 2C C C The compound according to claim 1, which is selected from the group consisting of: (1) 8-(2,2-dimethylpropyl)-7-oxo-5,6,7,8-tetrahydropyrimido[4,5-d]pyrimidine-2-carbonitrile, (2) 1-(2,2-dimethylpropyl)-2-(4-methoxybenzyl)-3-oxo-2,3-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (3) 1-(2,2-dimethylpropyl)-3-[(4-methoxybenzyl)oxy]-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (4) 4-(2,2-dimethylpropoxy)-1,3-benzothiazol-2-carbonitrile, (5) 3-(4-biphenylylmethoxy)-1-(2,2-dimethylpropyl)-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (6) 2-(4-biphenylylmethyl)-1-(2,2-

cyclic group containing
m or a nitrogen atom; n
ame or different, in
, a salt thereof, a solvate
a C5-7 monocyclic
ven-membered
cted from an oxygen
m 1, wherein ring A is a
rahydropyrimidine,
dihydropyridazine, pyridazine, dihydropyrimidine, dihydropyrazine, dihydrothiazine, pyrazole, dihydropyrazole, pyrrole, imidazole, triazole, thiophene, furan, dihydrofuran, oxadiazine, tetrahydrodiazepine and diazepane. The compound according to claim 1, wherein ring B is a ring selected from pyrrole, imidazole, pyrazole, thiazole, oxazole, pyridine, pyrimidine, dihydrotriazine, pyrazine and dihydropyrimidine. The compound according to claim 1, wherein the compound of formula (I) is 5,6,7,8-tetrahydropyrimido[4,5-d]pyrimidine-2-carbonitrile, pyrazolo[1,5-a]pyrimidine-5-carbonitrile, 2,3-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, pyrazolo[1,5-a][1,3,5]triazine-2-carbonitrile, 1H-pyrimido[4,5-e][1,3,4]oxadiazine-7-carbonitrile, 1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, imidazo[1,2-a]pyrimidine-2-carbonitrile, 1,3-benzothiazol-2-carbonitrile, 6,7,8,9-tetrahydro-5H-pyrimido[4,5-e][1,4]diazepine-2-carbonitrile, 5H-pyrrolo[3,2-d]pyrimidine-2-carbonitrile, pyrido[2,3-d]pyrimidine-2-carbonitrile, 5,7-dihydrofuro[3,4-d]pyrimidine-2-carbonitrile, 6,7-dihydro-5H-cyclopenta[d]pyrimidine-2-carbonitrile, 9H-purine-2-carbonitrile, or 1,3-benzoxazole-2-carbonitrile. The compound according to claim 1, which is a compound of formula (I-A) or formula(I-B) wherein R is a hydrogen atom or a substituent; n1 is 0, or an integer of from 1 to 3; and R is wherein T, T, T and T each is independently a bond or a spacer having from 1 to 10 atoms of the principle chain; ring 1, ring1 and ring2 each is
bstituent, and other symbols have
to claim 6, wherein R is a
E each is independently a bond
C(=O)-, -C(=O)NR-, - NRC(=O)-,
a hydrogen atom or a
containing a nitrogen atom which
herein -T- is -E-E-E- in which all
clic carbocyclic group which may
hich may have a substituent(s).1B
same meanings as described in
ring 1 and/or ring 2 is (1) C3-10
red monocyclic or bicyclic
heterocyclic group which may have a substituent(s).1C 3 2 1 2C C C The compound according to claim 1, which is selected from the group consisting of: (1) 8-(2,2-dimethylpropyl)-7-oxo-5,6,7,8-tetrahydropyrimido[4,5-d]pyrimidine-2-carbonitrile, (2) 1-(2,2-dimethylpropyl)-2-(4-methoxybenzyl)-3-oxo-2,3-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (3) 1-(2,2-dimethylpropyl)-3-[(4-methoxybenzyl)oxy]-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (4) 4-(2,2-dimethylpropoxy)-1,3-benzothiazol-2-carbonitrile, (5) 3-(4-biphenylylmethoxy)-1-(2,2-dimethylpropyl)-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (6) 2-(4-biphenylylmethyl)-1-(2,2-dimethylpropyl)-3-oxo-2,3-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (7) 1-(2,2-dimethylpropyl)-3-oxo-2-(2-thienylmethyl)-2,3-dihydro-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (8) 1-(2,2-dimethylpropyl)-3-[2-(4-morpholinyl)ethoxy]-1H-pyrazolo[3,4-d]pyrimidine-6-carbonitrile, (9) 9-(2,2-dimethylpropyl)-6-(4-methoxybenzyl)-7-oxo-6,7,8,9-tetrahydro-5H-pyrimido[4,5-e][1,4]diazepine-2-carbonitrile, (10) 8-(2,2-dimethylpropyl)-6-(4-methoxybenzyl)-7-oxo-5,6,7,8-tetrahydropyrimido[4,5-d]pyrimidine-2-carbonitrile, (11) 4-[(2,2-dimethylpropyl)amino]pyrido[2,3-d]pyrimidine-2-carbonitrile, (12) 1-(2,2-dimethylpropyl)-3-{4-[(4-methyl-1-piperazinyl)methyl]phenyl}-1H-pyrimido[4,5-e][1,3,4]oxadiazine-7-carbonitrile, (13) 2-[6-cyano-1-(2,2-dimethylpropyl)-3-oxo-1,3-dihydro-2H-pyrazolo[3,4-d]pyrimidin-2-yl]-N-[2-(dimethylamino)ethyl]acetamide, (14) 4-[(2,2-dimethylpropyl)amino]-5,7-dihydrofuro[3,4-d]pyrimidine-2-carbonitrile, and (15) 4-[(2,2-dimethylpropyl)amino]-6,7-dihydro-5H-cyclopenta[d]pyrimidine-

But: Huge chemical Name Regions in the same Patent

and which may be partially saturated or fully saturated, . Three- to fifteen-membered mono-, polycyclic aromatic heterocyclic group, and polycyclic heterocyclic group having spiro bond, and polycyclic bridged heterocyclic group which contain 1 to 5 hetero atoms selected from an oxygen atom(s), a nitrogen atom(s) and a sulfur atom(s) which may be oxidized, and which may be partially saturated or fully saturated include, for example, pyrrole, imidazole, triazole, tetrazole, pyrazole, pyridine, pyrazine, pyrimidine, pyridazine, triazine, azepine, diazepine, furan, pyran, oxepine, thiophene, thiopyran, thiepine, oxazole, isoxazole, thiazole, isothiazole, furazan, oxadiazole, oxazine, oxadiazine, oxazepine, oxadiazepine, thiadiazole, thiazine, thiadiazine, thiazepine, thiadiazepine, indole, isoindole, indolizine, benzofuran, isobenzofuran, benzothiophene, isobenzothiophene, dithianaphthalene, indazole, quinoline, isoquinoline, quinolizine, purine, phthalazine, pteridine, naphthyridine, quinoxaline, quinazoline, cinnoline,



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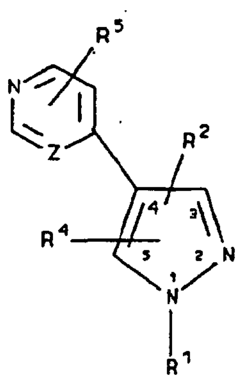
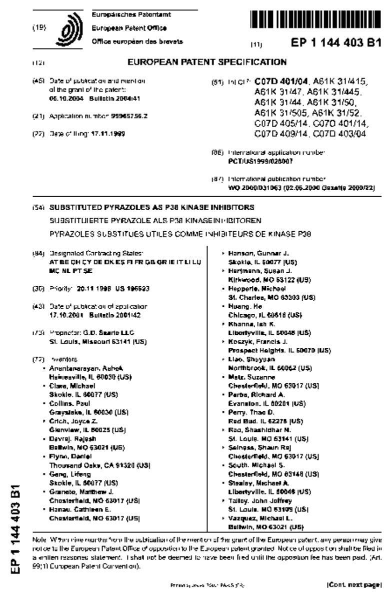
- 946 pages
- EP 1144403 B1
- SUBSTITUTED PYRAZOLES AS P38 KINASE INHIBITORS
- G.D. Searle LLC



(IXA)



(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 1 144 403 B1

(12) EUROPEAN PATENT SPECIFICATION

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(21) Application number: 99965756.2

(22) Date of filing: 17.11.1999

(51) Int Cl.7: C07D 401/04, A61K 31/415, A61K 31/47, A61K 31/445, A61K 31/44, A61K 31/50, A61K 31/505, A61K 31/52, C07D 405/14, C07D 401/14, C07D 409/14, C07D 403/04

(86) International application number: PCT/US1999/026007

(87) International publication number: WO 2000/031063 (02.06.2000 Gazette 2000/22)

(54) SUBSTITUTED PYRAZOLES AS P38 KINASE INHIBITORS
SUBSTITUIERTE PYRAZOLE ALS P38 KINASEINHIBITOREN
PYRAZOLES SUBSTITUES UTILES COMME INHIBITEURS DE KINASE P38

(84) Designated Contracting States: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

(30) Priority: 20.11.1998 US 196623

(43) Date of publication of application: 17.10.2001 Bulletin 2001/42

(73) Proprietor: G.D. Searle LLC
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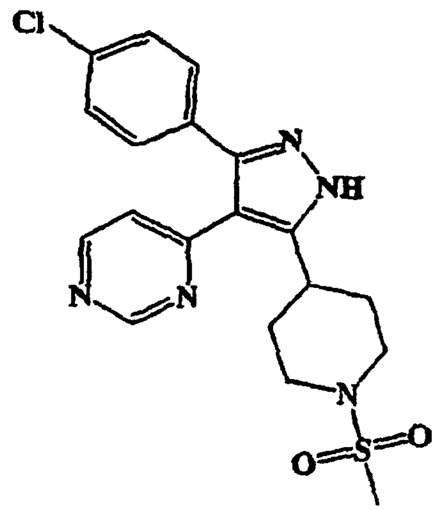
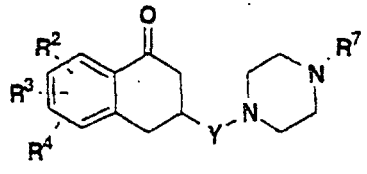
(Cont. next page)

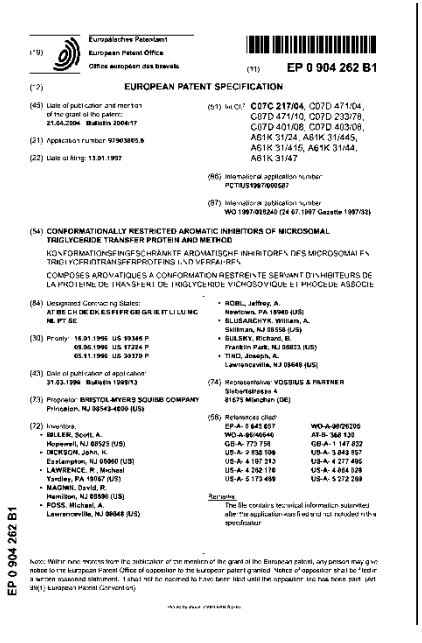
EP 1 144 403 B1



Category: largest Document (II)

- 715 pages
- EP 0904262 B1
- CONFORMATIONALLY RESTRICTED AROMATIC INHIBITORS OF MIRCOSOMAL TRIGLYCERIDE TRANSFER PROTEIN AND METHOD
- BRYSTOL-MYERS SQUIBB





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(54) CONFORMATIONALLY RESTRICTED AROMATIC INHIBITORS OF MICROSOMAL TRIGLYCERIDE TRANSFER PROTEIN AND METHOD

KONFORMATIONSEINGESCHRÄNKTE AROMATISCHE INHIBITOREN DES MIKROSOMALEN TRIGLYCERIDTRANSFERPROTEINS UND VERFAHREN

COMPOSES AROMATIQUES A CONFORMATION RESTREINTE SERVANT D'INHIBITEURS DE LA PROTEINE DE TRANSFERT DE TRIGLYCERIDE MICROSOMIQUE ET PROCEDE ASSOCIE

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(56) References cited:

EP-A- 0 643 057	WO-A-9626205
WO-A-9640640	AT-B- 368 120
GB-A- 773 758	GB-A- 1 147 832
US-A- 3 938 596	US-A- 3 843 957
US-A- 4 197 313	US-A- 4 277 486
US-A- 4 262 170	US-A- 4 864 828
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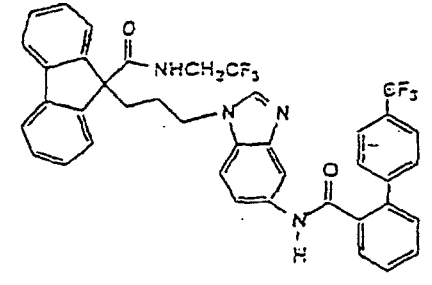

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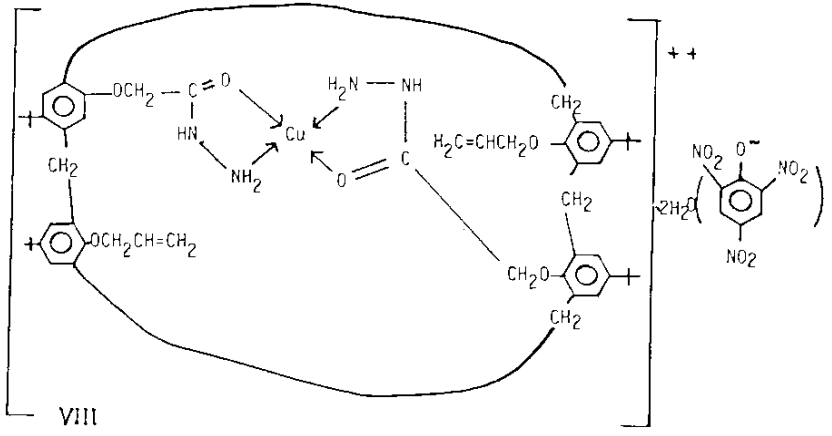
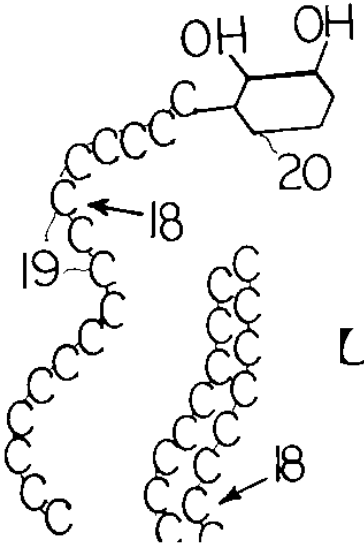
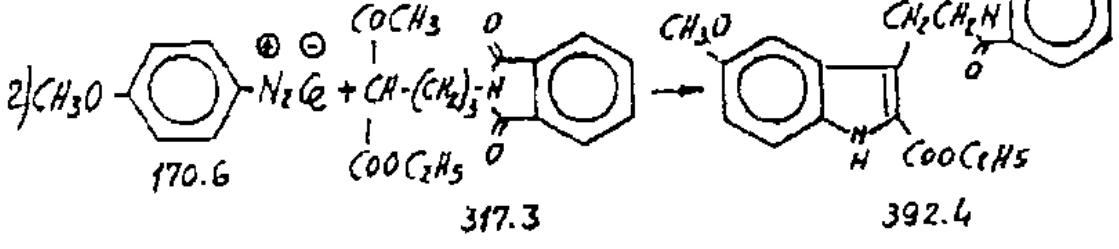
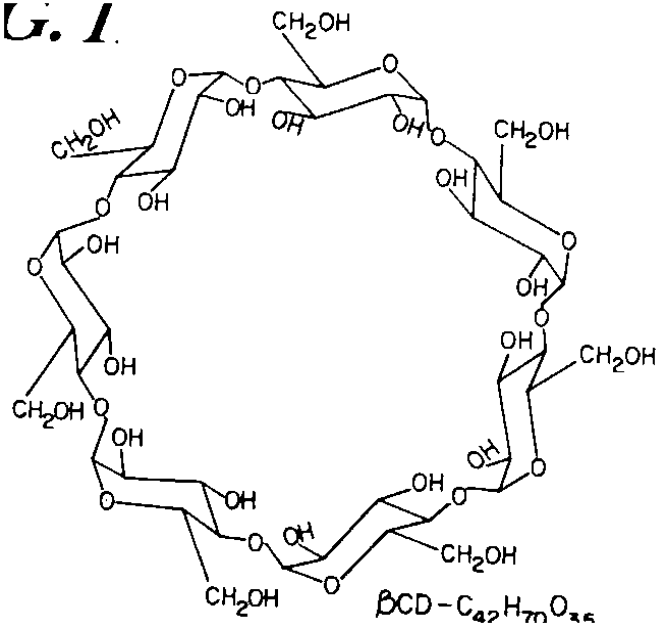
Category: That's Organic Chemistry









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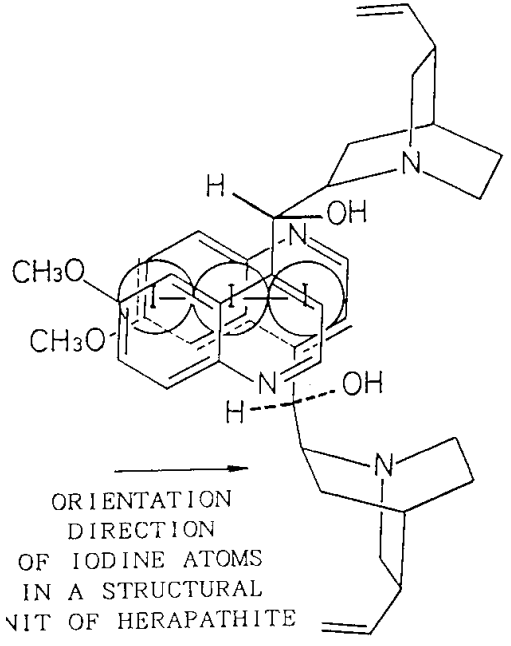
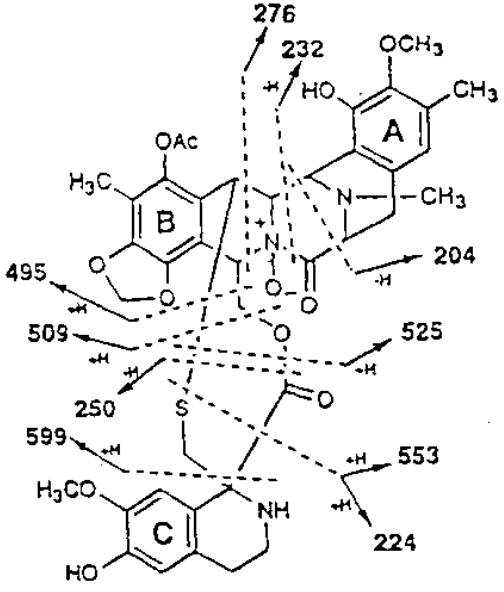
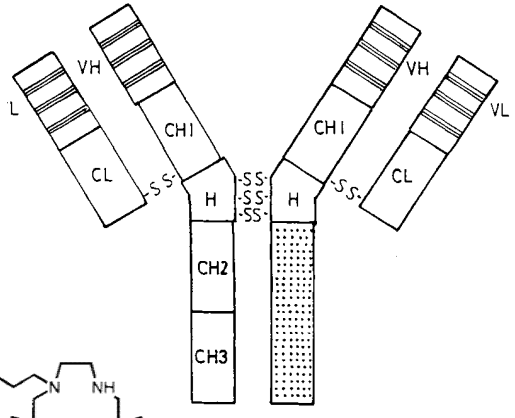
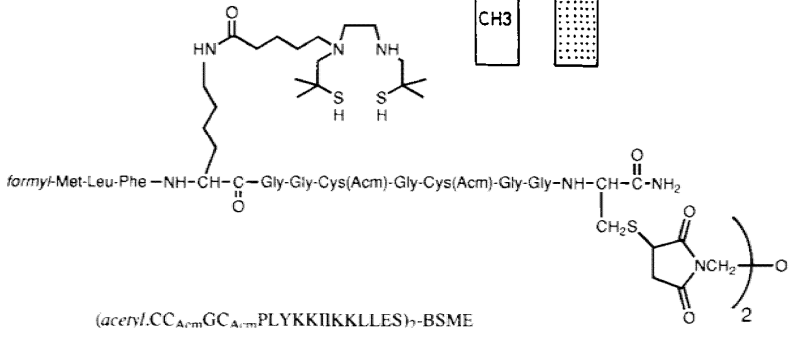
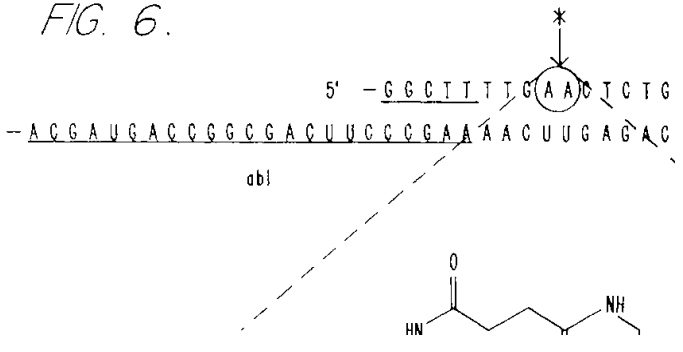


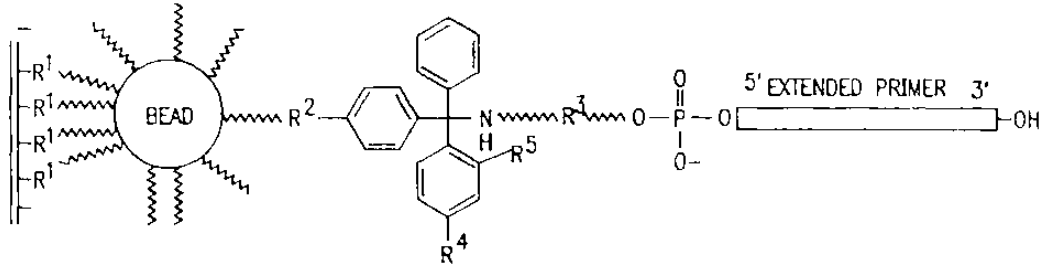
FIG. 6.











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Conclusions

- Image reconstruction is an ongoing effort
- Patents offer a lot of challenges
- In need of critical assessments and gold standards
  - Image reconstruction
  - Retrieval tasks
  - Hardware infrastructures
- In need of strategies
  - Deal with reconstruction errors
  - Extended file formats & search algorithms
  - Result visualizations

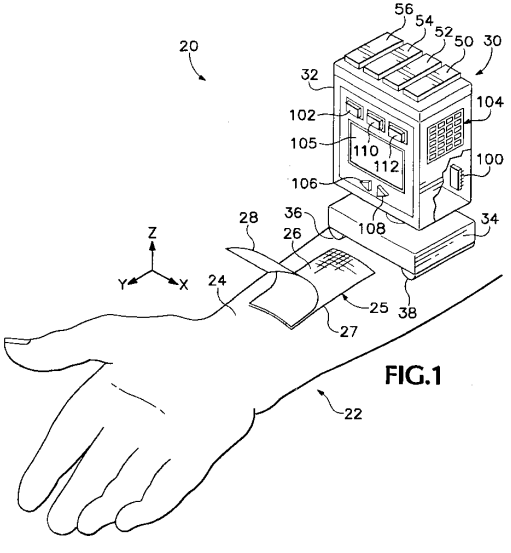


FIG.1

chemocr
chemical compound reconstruction

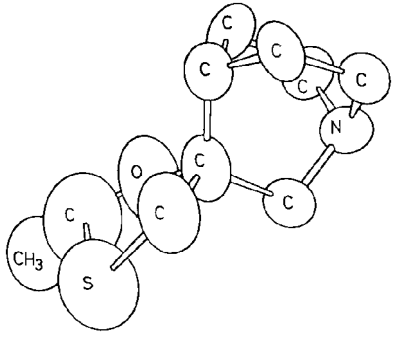
http://www.scai.fraunhofer.de/chemocr

InfoChem

Hans Kraut
Dr. Josef Eiblmaier
Dr. Peter Löw

THESEUS

Dr. Jörn Kohlhammer



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