STN®

THE CHOICE OF PATENT EXPERTS™

ReaxysFile™ on STN:

Reactions

ReaxysFile™ on STN: Reactions

Introduction

Chemical reactions such as combustion in the fire, fermentation and the reduction of ores to metals are known since ancient times. Initial theories of transformation of materials were developed by Greek philosophers, such as the Four-Element Theory stating that any substance is composed of the four basic elements – fire, water, air and earth. In the Middle Ages, chemical transformations were studied by Alchemists. They attempted, in particular, to convert lead into gold. Regarding the organic chemistry, it was long believed that compounds obtained from living organisms were too complex to be obtained synthetically. According to the concept of "vitalism", organic matter was endowed with a "vital force" and distinguished from inorganic materials. This separation ended by the synthesis of urea from inorganic precursors in 1828.

The production of chemical substances that do not normally occur in nature has long been tried, with the development of the lead chamber process in 1746 and the Leblanc process, chemical reactions became implemented into the industry. Nowadays, the chemical and pharmaceutical industry represents an important economic activity. To protect developed products and evaluate the freedom-to-operate, reactions from patents became more and more important over the last years.

ReaxysFile includes detailed information on reactions associated with a substance from journals and patents.

Fig.1: Reaction information derived from a patent

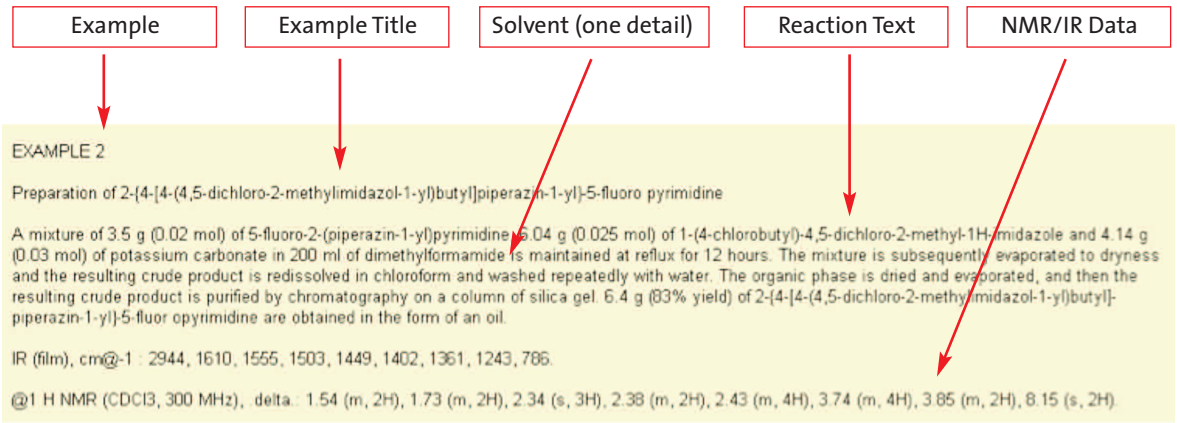

Fig.2: Corresponding part of the database record (RX)

```
Reaction:
RX
      Reaction ID:                        22874415
      Reactant AN (.RAN):                 13197503, 5336292
      Reactant (.RCT):                    1-(4-chlorobutyl)-4,5-dichloro-2-methyl-1H
                                          -imidazole,
                                          5-fluoro-2-(piperazin-1-yl)-pyrimidine
      Product AN (.PAN):                  13218853
      Product (.PRO):                     2-<4-<4-(4,5-dichloro-2-methylimidazol-1-y
                                          l)butyl>-1-piperazinyl>-5-fluoropyrimidine
      React. Struct. Keywords (.SKW):     mapped reaction
      Record type (.RTYP):                full reaction, has preparation
      Number of Bond Changes (.NBC):      3
      No. of React. Details (.NVAR):      2
      Preparation reactants (.BLB):       13197503, 5336292, 13218853
      Det. React. reactants (.BLC):       13197503, 5336292, 13218853
      No. of References (.NUMREF):        2

Reaction Details:
RX
      Reaction RID (.RID):                22874415.1
      Reaction Classification (.CL):      Preparation
      Yield (.YDT):                       83 percent
      Reagent (.RGT):                     potassium carbonate
      Solvent (.SOL):                     N,N-dimethyl-formamide
      Time (.TIM):                        12
      Other Conditions (.COND):           Heating / reflux
      Location (.LCN):                    Page column 3-4
      Example title (.TI):                EXAMPLE 2
      Fulltext of reaction (.TXT):        Preparation of
                                          2-<4-<4-(4,5-dichloro-2-methylimidazol-1-y
                                          l)butyl>piperazin-1-yl>-5-fluoropyrimidine
                                          <br/>A mixture of 3.5 g (0.02 mol) of
                                          5-fluoro-2-(piperazin-1-yl)pyrimidine,
                                          6.04 g (0.025 mol) of
                                          1-(4-chlorobutyl)-4,5-dichloro-2-methyl-1H
                                          -imidazole and 4.14 g (0.03 mol) of
                                          potassium carbonate in 200 ml of
                                          dimethylformamide is maintained at reflux
                                          for 12 hours.. <br/>The mixture is
                                          subsequently evapourated to dryness and the
                                          resulting crude product is redissolved in
                                          chloroform and washed repeatedly with
                                          water.. <br/>The organic phase is dried
                                          and evapourated, and then the resulting
                                          crude product is purified by
                                          chromatography on a columm of silica gel.
                                          6.4 g (83percent yield) of
                                          2-<4-<4-(4,5-dichloro-2-methylimidazol-1-y
                                          l)butyl>piperazin-1-yl>-5-fluoropyrimidine
                                          are obtained in the form of an oil.
                                          <br/>IR (film), cm-1: 2944, 1610, 1555,
                                          1503, 1449, 1402, 1361, 1243, 786. <br/>1H
                                          NMR (CDCl3, 300 MHz), .delta.: 1.54 (m,
                                          2H), 1.73 (m, 2H), 2.34 (s, 3H), 2.38 (m,
                                          2H), 2.43 (m, 4H), 3.74 (m, 4H), 3.85 (m,
                                          2H), 8.15 (s, 2H). <br/>
      Example label (.LB):                2
      Product AN (.PRAN):                 13218853
      Reactant AN (.RCAN):                4267587
      Solvent AN (.SOLAN):                605365
      Number of R. steps (.STP):          1
      Yield numerical (.YDN):             83
      Product (.YPRO):                    2-<4-<4-(4,5-dichloro-2-methylimidazol-1-y
                                          l)butyl>-1-piperazinyl>-5-fluoropyrimidine

      Reference(s):
      1. Patent: Methods for preparation of
         2-(4-(4-(4,5-dichloro-2-methylimidazol-1-yl)butyl)-1-piperazinyl)-5-
         fluoropyrimidine and salts thereof; …
```

2. Which Reaction Classes are Indexed (/RX.CL)?

ReaxysFile distinguishes between the following classes:

- Chemical behaviour
- Preparation

A reaction is classified either as "Preparation" or "Chemical Behaviour" depending on whether the preparative methods of a specific compound or its chemical behaviours are the aim of the investigation.

For “Chemical Behaviour”, there are quantitative results pertaining to the course of a reaction; at least one of the attributes presented should be listed in the field "Subject Studied" (/RX.SUBJ).

- Markush reaction

  Markush reactions mostly have only a few reaction details like reagent or temperature. Reaction Structure Keywords (/RX.SKW) often indicate “zero reaction” or “failed mapping”.

- Multi-step reaction

  Multi step reactions are a special type of preparations. The details for several reaction steps are given.

- Preparation (half reaction)

  Half reactions are defined by the fact, that either only educts or only products are characterized by an Accession Number.

3. Patent vs. Journal

3.1. Patent documents published before Dec 2003

Reactions are indexed from the example section. For almost all those reactions, the example text is available in the database. Reagents, solvents, and catalysts are often (but not always) identified and searchable via Accession number or Chemical name. Analogous reactions are often indexed as half-reactions with a product identification and reaction text.

3.2. Patent documents with publication date Dec 2003 ongoing

Reactions are indexed from the complete patent text have a very high indexing depth. Here all reaction partners - reactants, reagents, catalysts, solvents, and products – have detailed substance identification. Analogous reactions are often indexed as half-reactions with a product identification and reaction text.

3.3. Journals

Reactions derived from journals do not include property fields with extensive text like RX.TXT.

4. Typical Questions

- Determine if the chemical behaviour of a substance has been described in the past chemical literature
- Find syntheses for a given substance
- Search for members of a substance family which are used as catalysts
- Find comprehensive physical data of intermediates of a specific reaction

5. Ways to Gain Reaction Information

Each reaction is a separate database record. The **Reaction** Identification Data are stored in various fields. These contain the keys to the information that has been used to register the reaction. Reactants and Products can be searched by structure, name or Accession Number. The Reaction Identification Number is the registry number of the reaction and is hence unique.

```
Reaction:
RX
      Reaction ID:                    30260620
      Reactant AN (.RAN):             3633585, 969839
      Reactant (.RCT):                mono-methyl malonate potassium salt,
                                      cyclopropanecarboxylic acid
      Product AN (.PAN):              2802889
      Product (.PRO):                 methyl-3-cyclopropyl-3-oxopropanoate
      React. Struct. Keywords (.SKW): mapped reaction
      Record type (.RTYP):            full reaction, has preparation
      Number of Bond Changes (.NBC):  6
      No. of React. Details (.NVAR):  1
      Preparation reactants (.BLB):   3633585, 969839, 2802889
      Det. React. reactants (.BLC):   3633585, 969839, 2802889
      No. of References (.NUMREF):    1
```

The parameter data, such as solvent, temperature and further conditions, belonging to a particular variation of a reaction is stored in the fact **Reaction Details**. For any registered reaction there can be several variations present in the database whose total number is given in the field "**Number of Reaction Details**". Mostly all fields are searchable.

```
Reaction Details:
RX
      Reaction RID (.RID):            30260620.1
      Reaction Classification (.CL):  Preparation
      Reagent (.RGT):                 1,1'-carbonyldiimidazole, magnesium
                                      chloride
      Solvent (.SOL):                 tetrahydrofuran
      Location (.LCN):                scheme or table
      Reactant AN (.RCAN):            6826, 8128169
      Solvent AN (.SOLAN):            102391
      Number of R. steps (.STP):      1
      Reference(s):
      1. Qin, Jun; Rao, Ashwin; Chen, Xiao; Zhu, Xiaohong; Liu, Zhidan; Huang,
         Xianhai; Degrado, Sylvia; Huang, Ying; Xiao, Dong; Aslanian, Robert;
         Palani, Anandan; Cheewatrakoolpong, Boonlert; Zhang, Hongtao;
         Greenfeder, Scott; Farley, Constance; Cook, John; Kurowski, Stan; Li,
         Qiu; Van Heek, Margaret; Chintala, Madhu; Wang, Ganfeng; Hsieh,
         Yunsheng; Li, Fangbiao, Medicinal Chemistry letters, CODEN: AMCLCT,
         2(2), <2011>, 171 - 176
```

Note: It is important to know that searches performed in the area of Reaction Identification Data and Reaction Details will result in an answer set of reactions. Searches with a combination of substance and reaction terms cannot directly be executed. Crossover from substance to reaction part of the file is achieved by identifying Accession Numbers and searching them as reactants or products. To identify substances with reaction information, use RX/FA.

6. Good to Know

- Be careful with restrictions to a specific yield. RX.YDT is a numeric field, but has variable content (e.g. fixed ranges). Optical yield (RX.YDO) is in no way related to the “chemical” yield of a reaction. In a reaction involving chiral reactants and products, the optical yield is the ratio of the optical purity of the product to that of the precursor, reactant or catalyst.
- To keep terms within one reaction, use (P) operator.
- Using SELECT for crossover (SUB <->RX) may recommend SET POST OFF.
- There is a “super search field RX” which contains the several sub-fields, e.g. solvent or catalyst.
- The Basic Index (BIRX) for reactions contains single terms from all fields containing chemical names, Accession Numbers or text.

7. Examples

Example 1: Search for reactions of single substances with a benzotriazole structure element described as catalysts (restricted to patents).

Note: Catalysts and organometallic compounds are indexed by structure from patents published since Dec 2003. Before the publication date December 2003 they are indexed by structure if they are commercially available. If they are not commercially available, they are indexed by name. For comprehensive results, use both structure search and chemical name (segment) search.

```
Uploading C:\STN Express 8.5\Queries\Benzotriazole Catalysts.str

L33     STRUCTURE UPLOADED

=>  133 full
FULL SEARCH INITIATED 14:42:23
FULL SCREEN SEARCH COMPLETED -    26056 TO ITERATE

100.0% PROCESSED    26056 ITERATIONS                          13500 ANSWERS
SEARCH TIME: 00.00.06

L34       13500 SEA SSS FUL L33

=>  s l34 or (benzotriazol or benzotriazole)/cns and rx/fa and nf=1 and p/dt and
            py>2002
      15864973 RX/FA
               (RX/FA.RX)
L36      14368 L34 OR (BENZOTRIAZOL OR BENZOTRIAZOLE)/CNS AND RX/FA AND NF=1 AND
               P/DT AND PY>2002

=> transfer l36 an 1- /rx.caan
L37          TRANSFER L36 1- AN :    14368 TERMS
L38         832 L37/RX.CAAN

=> d

L38  ANSWER 1 OF 832 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN


Reaction:
RX
     Reaction ID:                    30015646
     Reactant AN (.RAN):             14423552, 21007735
     Reactant (.RCT):                5-chloro-6-
                                     <(1-methylethyl)oxy>-3-pyridinecarboxylic
                                     acid,
                                     3-bromo-2-ethyI-N-hydroxybenzenecarboximid
                                     amide
     Product AN (.PAN):              21007775
     Product (.PRO):                 5-<3-(3-bromo-2-ethylphenyl)-1,2,4-oxadiaz
                                     ol-5-yl>-3-chloro-2-<(1-methylethyl)oxy>py
                                     ridine
     React. Struct. Keywords (.SKW): mapped reaction
     Record type (.RTYP):            full reaction, has preparation
     Number of Bond Changes (.NBC):  5
     No. of React. Details (.NVAR):  1
     Preparation reactants (.BLB):   14423552, 21007735, 21007775
     Det. React. reactants (.BLC):   14423552, 21007735, 21007775
     No. of References (.NUMREF):    1

Reaction Details:
RX
     Reaction RID (.RID):            30015646.1
     Reaction Classification (.CL):  Preparation
     Nr. of Stages (.SNR):           3
     Location (.LCN):                Page/Page column 37-38
     Fulltext of reaction (.TXT):    Description for D23
                                     5-<3-(3-bromo-2-ethylphenyl)-1,2,4-oxadiaz
                                     ol-5-yl>-3-chloro-2-<(1-
                                     methylethyl)oxy>pyridine
                                     (D23).delta.-chloro-.beta.-
                                     i-methylethyOoxyl-S-pyridinecarboxylic
                                     acid (2.0 g), EDCI (3.56 g), HOBT (2.84 g)
                                     were dissolved in THF (50 ml). After the
                                     mixture was stirred for 10 mins at RT, a
                                     solution of
                                     3-bromo-2-ethyl-.lambda./-hydroxybenzeneca
                                     rboximidamide (1.62 g) in THF (50 ml) was
                                     added slowly. The obtained mixture was
                                     stirred for further 2 hours at room
                                     temperature. LCMS show only one
                                     intermediate was found. After addition of
                                     TBAF (12.6 g), the reaction mixture was
```

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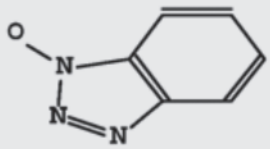
                                    heated to 80 0C for 2 days. The reaction
                                    was cooled down to room temperature,
                                    Evapourate off the solvent and added with
                                    EtOAc (100 ml). The organic solution was
                                    washed with saturated aqueous sodium
                                    dicarbonate solution (twice) and water
                                    (twice). After removal of the solvent,
                                    residue was purified by flash column
                                    (Hexane: DCM= 10:1) to afford a off white
                                    solid. LCMS confirmed as the desired
                                    compound 5-<3-(3-bromo-2-ethylphenyl)-1
                                    ,2,4-
                                    oxadiazol-5-yl>-3-chloro-2-<(1-methylethyl
                                    )oxy>pyridine (2.41 g). .delta.H (CDCI3,
                                    400 MHz): 1.28(3H1 t), 1.46 (6H, d),
                                    3.13-3.17(2H, m), 5.48-5.52 (1H, m),
                                    7.18-7.22 (1 H, dd), 7.73-7.75 (1H, dd),
                                    7.87-7.89 (1H, dd), 8.38 (1H, d), 8.88
                                    (1H, d).MS (ES): C18Hi7BrCIN3O2 requires
                                    421; found 422.2 (M+H+).
      Example label (.LB):          D23
      Number of R. steps (.STP):    1
      Stage (.STG):                 1
      Reagent (.RGT):               1-ethyl-(3-(3-dimethylamino)propyl)-carbod
                                    iimide hydrochloride
      Stage reactant (.SRCT):       5-chloro-6-
                                    <(1-methylethyl)oxy>-3-pyridinecarboxylic
                                    acid
      Stage Reactant AN (.SRAN):    14423552
      Catalyst (.CAT):              benzotriazol-1-ol
      Solvent (.SOL):               tetrahydrofuran
      Time (.TIM):                  0.166667
      Temperature (.T):             20 Cel
      Catalyst AN (.CAAN):          4515
      Reactant AN (.RCAN):          5764110
      Solvent AN (.SOLAN):          102391
      Stage (.STG):                 2
      Stage reactant (.SRCT):       3-bromo-2-ethyI-N-hydroxybenzenecarboximid
                                    amide
      Stage Reactant AN (.SRAN):    21007735
      Solvent (.SOL):               tetrahydrofuran
      Time (.TIM):                  2
      Temperature (.T):             20 Cel
      Solvent AN (.SOLAN):          102391
      Stage (.STG):                 3
      Reagent (.RGT):               tetrabutyl ammonium fluoride
      Solvent (.SOL):               tetrahydrofuran
      Time (.TIM):                  48
      Temperature (.T):             80 Cel
      Reactant AN (.RCAN):          3570522
      Solvent AN (.SOLAN):          102391
      Reference(s):
      1. Patent: 5-MEMBERED HETEROARYL DERIVATIVES USED AS SPHINGOSINE
         1-PHOSPHATE RECEPTOR AGONISTS; for details see special display format
         ALLPAT

=> s 4515/an
L39           1 4515/AN

=> d

L39  ANSWER 1 OF 1 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN

      Accession Number (AN):        4515
      Basic Pref. RN (BPR):         2592-95-2
      CAS Reg. No. (RN):            2592-95-2
      Chemical Name (CN):           benzotriazol-1-ol,
                                    N-hydroxy-benzotriazole,
                                    1-hydroxy-1H-1,2,3-benzotriazole,
                                    1-hydroxybenzotriazole hydrate,
                                    1-hydroxy-1,2,3-benzotriazole,
                                    hydroxy-1,2,3-benzotriazole,
                                    1-hydroxy-1H-benzotriazole
      Autonom Name (AUN):           Benzotriazol-1-ol
      Lin. Struct. Formula (LSF):   (C6H4N3)OH
      Molec. Formula (MF):          C6 H5 N3 O
      Formula Weight (FW):          135.125
      InChi Key: (INCHI):           ASOKPJOREAFHNY-UHFFFAOYSA-N
      Alternate InChi Key: (AINCHI): ASOKPJOREAFHNY-UHFFFAOYAP
      Compound Type (CTYPE):        heterocyclic
      Markush Ref. Count (MARKREF): 15
      Entry Date (DED):             1988/06/27
      Update Date (DUPD):           2011/03/23
```



Field Availability:…

Example2:
Search for preparations of phenyl acrylic acid (“Zimtsäure”) with malonic acid as a reagent.
Note: Include multi-step reactions, there may be preparations listed. See the depth of indexing for records with PY>2003.

```
Uploading C:\STN Express 8.5\Queries\Zimtsaeure.str

L20      STRUCTURE UPLOADED

=> s l20 exa full
FULL SEARCH INITIATED 13:11:35
FULL SCREEN SEARCH COMPLETED -       272 TO ITERATE

100.0% PROCESSED       272 ITERATIONS                       48 ANSWERS
SEARCH TIME: 00.00.01

L21           48 SEA EXA FUL L20

=> sel an 1-
E1 THROUGH E48 ASSIGNED

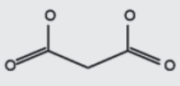
=> s e1-48/rx.pan
L22         799 (11126713/RX.PAN …

=> s malonic acid/cn
L23           2 MALONIC ACID/CN

=> d 2

L23  ANSWER 2 OF 2 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN

      Accession Number (AN):          1751370
      Basic Pref. RN (BPR):           141-82-2
      CAS Reg. No. (RN):              141-82-2
      Chemical Name (CN):             malonic acid,
                                      1,3-dihydroxy-1,3-propanedione,
                                      propanedioic Acid, propandioic acid,
                                      permalonic acid, maleic acid, MA
      Autonom Name (AUN):             Malonic acid
      Lin. Struct. Formula (LSF):     HOCOCH2COOH
      Molec. Formula (MF):            C3 H4 O4
      Formula Weight (FW):            104.062
      InChi Key: (INCHI):             OFOBLEOULBTSOW-UHFFFAOYSA-N
      Alternate InChi Key: (AINCHI):  OFOBLEOULBTSOW-CVXXDPDJCU
      Compound Type (CTYPE):          acyclic
      Markush Ref. Count (MARKREF):   14
      Entry Date (DED):               1989/02/27
      Update Date (DUPD):             2011/03/22
```



Field Availability: …

```
=> e a/rx.cl
**** START OF FIELD ****
E3            0  -->   A/RX.CL
E4      1237563        BEHAVIOUR/RX.CL
E5      1237563        CHEMICAL/RX.CL
E6      1237563        CHEMICAL BEHAVIOUR/RX.CL
E7      4858718        HALF/RX.CL
E8        28468        MARKUSH/RX.CL
E9        28468        MARKUSH REACTION/RX.CL
E10    11669504        MULTI/RX.CL
E11    11669504        MULTI-STEP REACTION/RX.CL
E12    16998108        PREPARATION/RX.CL
```

```
=> s e11-12 and 1751370/rx.ran (p) l22
L24          11 ("MULTI-STEP REACTION"/RX.CL OR PREPARATION/RX.CL) AND 1751370/R
                X.RAN (P) L22

=> d … rx

Reaction:
RX
      Reaction ID:                    598097
      Reactant AN (.RAN):             1751370, 471223
      Reactant (.RCT):                malonic acid, benzaldehyde
      Product AN (.PAN):              507757
      Product (.PRO):                 3-phenyl-2-propenoic acid
      React. Struct. Keywords (.SKW): mapped reaction
      Record type (.RTYP):            full reaction, has preparation
      Number of Bond Changes (.NBC):  6
      No. of React. Details (.NVAR):  12
      Preparation reactants (.BLB):   1751370, 471223, 507757
      Det. React. reactants (.BLC):   1751370, 471223, 507757
      No. of References (.NUMREF):    12
…
Reaction Details
RX
      Reaction RID (.RID):            598097.11
      Reaction Classification (.CL):  Preparation
      Nr. of Stages (.SNR):           2
      Location (.LCN):                experimental part
      Number of R. steps (.STP):      1
      Stage (.STG):                   1
      Reagent (.RGT):                 piperidine, pyridine
      Stage reactant (.SRCT):         malonic acid, benzaldehyde
      Stage Reactant AN (.SRAN):      1751370, 471223
      Other Conditions (.COND):       Reflux
      Reaction Type (.TYP):           Knoevenagel condensation
      Reactant AN (.RCAN):            102438, 103233
      Stage (.STG):                   2
      Reagent (.RGT):                 formic acid
      Solvent (.SOL):                 ethyl acetate, Petroleum ether
      Reactant AN (.RCAN):            1209246
      Solvent AN (.SOLAN):            506104, 8400700
      Reference(s):
      1. Zou, Hongbin; Wu, Hao; Zhao, Yu; Stoeckigt, Joachim; Yu, Yongping;
         Zhang, Xiangnan; Lou, Yijia, Bioorganic and Medicinal Chemistry, CODEN:
         BMECEP, 18(17), <2010>, 6351 - 6359
RX
      Reaction RID (.RID):            598097.12
      Reaction Classification (.CL):  Preparation
      Reagent (.RGT):                 piperidine, pyridine
      Reaction Type (.TYP):           Doebner-Knoevenagel condensation
      Location (.LCN):                body text
      Reactant AN (.RCAN):            102438, 103233
      Number of R. steps (.STP):      1
      Reference(s):
      1. Rodrigues-Santos, Claudio E.; Echevarria, Aurea, Tetrahedron Letters,
         CODEN: TELEAY, 52(2), <2011>, 336 - 340

Reaction:
RX
      Reaction ID:                    816786
      Reactant AN (.RAN):             1751370, 506810
      Reactant (.RCT):                malonic acid,
                                      N-(1-phenylmethylidene)methanamine
      Product AN (.PAN):              1905952, 3199979
      Product (.PRO):                 3-phenyl-2E-propenoic acid,
                                      (R,S)-3-N-methylamino-3-phenylpropionic
                                      acid
      React. Struct. Keywords (.SKW): nonmapped reaction
      Record type (.RTYP):            full reaction, has preparation
      Number of Bond Changes (.NBC):  5
      No. of React. Details (.NVAR):  1
      Preparation reactants (.BLB):   1751370, 506810, 1905952, 3199979
      Det. React. reactants (.BLC):   1751370, 506810, 1905952, 3199979
      No. of References (.NUMREF):    1

Reaction Details:
RX
      Reaction RID (.RID):            816786.1
      Reaction Classification (.CL):  Preparation
      Reagent (.RGT):                 ethanol
      Reactant AN (.RCAN):            1718733
      Number of R. steps (.STP):      1
      Reference(s):
      1. Johnson, Recueil des Travaux Chimiques des Pays-Bas, CODEN: RTCPA3, 48,
         <1929>, 874
```

Example 3:
Search for articles investigating xenobiotics. Start with substances having data for Dissociation Exponent, Solubility and Partition Constant Octanol/Water assigned. Restrict to products with cytotoxicity.

Note: Xenobiotics or environmental toxins are substances which are found in an organism but which is not normally produced or expected to be present in it. It can also cover substances which are present in much higher concentrations than are usual. Specifically, drugs such as antibiotics are xenobiotics in humans because the human body does not produce them itself, nor are they part of a normal diet.
It is recommended to check in /BIRX where the term xenobiotics occurs.

```
=> s (de and slb and pow)/fa and j/dt
         68902     DE/FA
        247799     SLB/FA
         19465     POW/FA
      36830864     J/DT
L1          884     (DE AND SLB AND POW)/FA AND J/DT

=> sel 1- an
E1 THROUGH E884 ASSIGNED

=> s e1-884/rx.pan

L2       147137 (10043857/RX.PAN…)

=> e a/rx.cl
**** START OF FIELD ****
E3            0 --> A/RX.CL
E4      1237563     BEHAVIOUR/RX.CL
E5      1237563     CHEMICAL/RX.CL
E6      1237563     CHEMICAL BEHAVIOUR/RX.CL
E7      4858718     HALF/RX.CL
E8        28468     MARKUSH/RX.CL
E9        28468     MARKUSH REACTION/RX.CL
E10   11669504     MULTI/RX.CL
E11   11669504     MULTI-STEP REACTION/RX.CL
E12   16998108     PREPARATION/RX.CL

=> e
E13    4858718     PREPARATION (HALF REACTION)/RX.CL
E14   16556672     REACTION/RX.CL
E15   11669504     STEP/RX.CL
**** END OF FIELD ****

=> s e11-12 and l2 and xenobiotics/rx.cond
L3          430 ("MULTI-STEP REACTION"/RX.CL OR PREPARATION/RX.CL) AND L2 AND
                XENOBIOTICS/RX.COND

=> d 5

L3   ANSWER 5 OF 430 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN

Reaction:
RX
      Reaction ID:                    27958358
      Reactant (.RCT):                crushed scrap tires
      Product AN (.PAN):              635760
      Product (.PRO):                 toluene
      React. Struct. Keywords (.SKW): half reaction
      Record type (.RTYP):            half reaction, has preparation
      Number of Bond Changes (.NBC):  0
      No. of React. Details (.NVAR):  2
      Preparation reactants (.BLB):   635760
      No. of References (.NUMREF):    1

Reaction Details:
RX
      Reaction RID (.RID):            27958358.1
      Reaction Classification (.CL):  Preparation (half reaction)
      Yield (.YDT):                   2.20 percent
      Reagent (.RGT):                 synthetic air
      Temperature (.T):               750 Cel
      Other Conditions (.COND):       Formation of xenobiotics
      Product AN (.PRAN):             635760
      Reactant AN (.RCAN):            19291633
      Number of R. steps (.STP):      1
      Yield numerical (.YDN):         2.2
      Product (.YPRO):                toluene
      Reference(s):
```

```
      1. Conesa, Juan A.; Martin-Gullon, I.; Font, R.; Jauhiainen, J.,
         Environmental Science and Technology, CODEN: ESTHAG, 38(11), <2004>,
         3189 - 3194
RX
      Reaction RID (.RID):            27958358.2
      Reaction Classification (.CL):  Preparation (half reaction)
      Yield (.YDT):                   2.86 percent
      Temperature (.T):               750 Cel
      Other Conditions (.COND):       Formation of xenobiotics
      Product AN (.PRAN):             635760
      Number of R. steps (.STP):      1
      Yield numerical (.YDN):         2.86
      Product (.YPRO):                toluene
      Reference(s):
      1. Conesa, Juan A.; Martin-Gullon, I.; Font, R.; Jauhiainen, J.,
         Environmental Science and Technology, CODEN: ESTHAG, 38(11), <2004>,
         3189 - 3194

=> d 5 allref

L3   ANSWER 5 OF 430 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN

      All References:
      ALLREF


       Reference:      Conesa, Juan A.; Martin-Gullon, I.; Font, R.; Jauhiainen,
                       J., Environmental Science and Technology, CODEN: ESTHAG,
                       38(11), <2004>, 3189 - 3194
       Title:          Complete Study of the Pyrolysis and Gasification of Scrap
                       Tires in a Pilot Plant Reactor
       Abstract:       The pyrolysis and gasification of tires was studied in a
                       pilot plant reactor provided with a system for condensation
                       of semivolatile matter. The study comprises experiments at
                       450, 750, and 1000 deg C both in nitrogen and 10percent
                       oxygen atmospheres. Analysis of all the products obtained
                       (gases, liquids, char, and soot) are presented. In the gas
                       phase only methane and benzene yields increase with
                       temperature until 1000 deg C. In the liquids the main
                       components are styrene, limonene, and isoprene. The solid
                       fraction (including soot) increases with temperature. Zinc
                       content of the char decreases with increasing temperature.

=> sel rx.pan 1-
E1 THROUGH E338 ASSIGNED

=> s e1-338/an and cytotoxicity/pharm.e
L4         137 (1307225/AN …)

=> d 1-10 cn
   (transcript edited)
      Chemical Name (CN):     polynuclear aromatic hydrocarbons; mixture…
      Chemical Name (CN):     polychlorinated biphenyls; mixture of,…
      Chemical Name (CN):     car-3-ene, δ3-carene,…
      Chemical Name (CN):     4-vinylsyringol, canolol,…
      Chemical Name (CN):     2,5-dihydroxyphenylcarboxylic acid,…
      Chemical Name (CN):     BCR-139, benzo<g,h,i>fluoranthene,…
      Chemical Name (CN):     cyclopenta<cd>pyrene,…
      Chemical Name (CN):     benzo<b>fluorene,…
      Chemical Name (CN):     Benzo<a>fluorene,11H-benzo<a>fluorene,…
      Chemical Name (CN):     4-Ethyl-2-methoxyphenol,…
```

Example 4:
Search for compositions of gold and platinum used as anode materials.
Note: Constituents in traces (<1) are specified as "o" in MF. The numerical values are indicated in LSF.

```
=> s au/els and pt/els and 2/elc
L1          206 AU/ELS AND PT/ELS AND 2/ELC

=> sel 1- an
E17 THROUGH E222 ASSIGNED

=> s e17-222/rx.pan
L2           23 (14950272/RX.PAN…)

=> e a/rx.cl
**** START OF FIELD ****
E3            0 --> A/RX.CL
E4      1237563      BEHAVIOUR/RX.CL
E5      1237563      CHEMICAL/RX.CL
E6      1237563      CHEMICAL BEHAVIOUR/RX.CL
E7      4858718      HALF/RX.CL
E8        28468      MARKUSH/RX.CL
E9        28468      MARKUSH REACTION/RX.CL
E10    11669504     MULTI/RX.CL
E11    11669504     MULTI-STEP REACTION/RX.CL
E12    16998108     PREPARATION/RX.CL …

=> s e11-12 and l2
L3           23 ("MULTI-STEP REACTION"/RX.CL OR PREPARATION/RX.CL) AND L2

=> d

L3   ANSWER 1 OF 23 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN


Reaction:
RX
      Reaction ID:                    28399696
      Reactant AN (.RAN):             11323097, 14292310
      Reactant (.RCT):                dihydrogen hexachloroplatinate, hydrogen
                                      tetrachloroaurate(III)
      Product AN (.PAN):              14950272
      Product (.PRO):                 platinum-gold
      React. Struct. Keywords (.SKW): nonmapped reaction
      Record type (.RTYP):            full reaction, has preparation
      Number of Bond Changes (.NBC):  4
      No. of React. Details (.NVAR):  1
      Preparation reactants (.BLB):   11323097, 14292310, 14950272
      Det. React. reactants (.BLC):   11323097, 14292310, 14950272
      No. of References (.NUMREF):    1

Reaction Details:
RX
      Reaction RID (.RID):            28399696.1
      Reaction Classification (.CL):  Preparation
      Reagent (.RGT):                 formic acid, ammonium formate
      Solvent (.SOL):                 water
      Reactant AN (.RCAN):            1209246, 3625095
      Solvent AN (.SOLAN):            3587155
      Number of R. steps (.STP):      1
      Reference(s):
      1. Wang, Jingpeng; Thomas, Dan F.; Chen, Aicheng, Chemical Communications
         (Cambridge, United Kingdom), CODEN: CHCOFS, <2008>, 5010 - 5012

=> sel rx.pan 1-
E1 THROUGH E16 ASSIGNED

=> s e1-16/an and 2/elc and elch/fa
L4            2 (14950272/AN OR 16837802/AN OR 17117706/AN OR 17461210/AN OR
                17461211/AN OR 17461212/AN OR 16524341/AN OR 16524560/AN OR 1652
                4793/AN OR 17961977/AN OR 18034326/AN OR 18034327/AN OR 18034328
                /AN OR 18034329/AN OR 18034330/AN OR 4173737/AN) AND 2/ELC AND
                ELCH/FA

=> d 1-

L4   ANSWER 1 OF 2 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN
```

```
      Accession Number (AN):          18034329
      Lin. Struct. Formula (LSF):     Pt0.55Au0.45
      Molec. Formula (MF):            Au0 Pt0
      Formula Weight (FW):            195.929
      Compound Type (CTYPE):          Alloy
      InChi Key: (INCHI):             JUWSSMXCCAMYGX-UHFFFAOYSA-N
      Alternate InChi Key: (AINCHI):  JUWSSMXCCAMYGX-UHFFFAOYAG
      Markush Ref. Count (MARKREF):   0
      Entry Date (DED):               2008/10/22
      Update Date (DUPD):             2010/10/31

      No structure diagram available for this Document

   Field Availability:

      Code      Name                                    Occurrence
      ========================================================
      AN        Accession Number                              1
      LSF       Linearized Structure Formula                  1
      MF        Molecular Formula                             1
      FW        Formula Weight                                1
      INCHI     InChi Key                                     1
      AINCHI    Alternate InChi Key                           1
      CTYPE     Compound Type                                 1
      MARKREF   Markush Reference Count                       1
      DED       Entry Date                                    1
      DUPD      Update Date                                   1
      CRYPH     Crystal Phase                                 2
      CSYS      Crystal System                                1
      ELCH      Electrochemistry Data                         1

   This substance also occurs in Reaction Documents:

      Code      Name                                    Occurrence
      ========================================================
      RX        Reaction Documents                            1
      RX.PAN    Product AN                                    1


Electrochemistry Data:
 Value       | Cell.Pot.   | Keyword                   |Ref.
 (ELCH)      | (.POT)      | (.KW)                     |
=============+=============+===========================+====
             |             | Behaviour as electrode    |1

Reference(s):
1. Stevens, D. A.; Rouleau, J. M.; Mar, R. E.; Bonakdarpour, A.; Atanasoski, R.
   T.; et al., Journal of the Electrochemical Society, CODEN: JESOAN, 154,
   <2007>, B566 - B576


L4   ANSWER 2 OF 2 REAXYSFILE COPYRIGHT 2012 Elsevier Properties SA. on STN

      Accession Number (AN):          14950272
      Chemical Name (CN):             platinum-gold
      Lin. Struct. Formula (LSF):     PtAu
      Molec. Formula (MF):            Au Pt
      Formula Weight (FW):            392.047
      Compound Type (CTYPE):          Alloy
      InChi Key: (INCHI):             JUWSSMXCCAMYGX-UHFFFAOYSA-N
      Alternate InChi Key: (AINCHI):  JUWSSMXCCAMYGX-UHFFFAOYAG
      Markush Ref. Count (MARKREF):   0
      Entry Date (DED):               2008/06/24
      Update Date (DUPD):             2010/11/01

      No structure diagram available for this Document

   Field Availability:

      Code      Name                                    Occurrence
      ========================================================
      AN        Accession Number                              1
      CN        Chemical Name                                 1
      LSF       Linearized Structure Formula                  1
      MF        Molecular Formula                             1
      FW        Formula Weight                                1
      INCHI     InChi Key                                     1
      AINCHI    Alternate InChi Key                           1
      CTYPE     Compound Type                                 1
      MARKREF   Markush Reference Count                       1
      DED       Entry Date                                    1
```

```
      DUPD      Update Date                                    1
      CRYPH     Crystal Phase                                  2
      ELCH      Electrochemistry Data                          1
      FINFO     Further Information                            3
      PSD       Patent Specific Data                           1
      QCC       Quantum Chemical Calculations                  3
      UVS       UV and Visible Spectrum                        1

    This substance also occurs in Reaction Documents:

      Code      Name                                      Occurrence
      ========================================================
      RX        Reaction Documents                             4
      RX.PAN    Product AN                                     4

Electrochemistry Data:
 Value       | Cell.Pot.   | Keyword                 |Ref.
 (ELCH)      | (.POT)      | (.KW)                   |
=============+=============+=========================+====
             |             | Behaviour as electrode  |1, 2

Reference(s):
1. Wang, Jingpeng; Thomas, Dan F.; Chen, Aicheng, Chemical Communications
   (Cambridge, United Kingdom), CODEN: CHCOFS, <2008>, 5010 - 5012
2. Gyenge, Elod; Atwan, Mohammed; Northwood, Derek, Journal of the
   Electrochemical Society, CODEN: JESOAN, 153, <2006>, A150 - A158
```

8. Summary

Ways to access reaction data:

- Crossover Accession Numbers from substance <=> reaction
- Combine reactants and/or products
- Combine reactant/product with reaction details
- SEARCH RX/FA for substances with reaction information
- SEARCH RXPRO/FA for substances which products in reaction records
- SEARCH RXREA/FA for substances which are reactants in reaction records
- DISPLAY HIT for reactions containing the requested information
- DISPLAY RX for all reactions of a substance (check Field Availability, use FRX for occurrence>50)

Appendix: Search and Display Fields for Reactions

Field Name	Search Code	Content/Comments/Type of Indexing
Field Availability	RX/FA	Search for availability of reactions for a specific substance
All ANs Reaction	/RX.AAN	Super Search Field, contains RX.RAN, RX.PAN, RX.SRAN , RX.CAN, RX.CAAN, RX.BLC, RX.BLC
Catalyst	/RX.CAT	Catalysts are compounds that do not appear in the stoichiometric equation of the reaction. They only influence the rate of the reaction. If it is not clear from the publication whether the compound is used as a reagent or a catalyst it is entered as a reagent.
Reaction Classification	/RX.CL	A reaction is classified either as "Preparation" or "Chemical Behaviour" depending on whether the preparative methods of a specific compound or its chemical behaviours are the aim of the investigation. Use EXPAND to explore further classifications.
Other Conditions	/RX.COND	Entries in the field “Other Conditions” are only given when there is important information that cannot be input in the other parameter fields, e.g. heating, UV irradiation. Particularly in the description of biochemical methods the biologically active materials (e.g. fungi, ferments, etc.) are entered in this field. Biological material (exactly defined) can be found in RX.RGT.
Reaction Identification	/RX.ID	The Reaction ID is assigned when a reaction is registered for the first time and is an unambiguous identifier.
Number of Reaction Details	/RX.NVAR	Numerical
Pressure	/RX.P	Numerical
Product AN	/RX.PAN	Accession Number(s) of reaction product(s)
pH Value	/RX.PH	Numerical
Product	/RX.PRO	Chemical name(s) of reaction product(s)
Prototype Reaction	/RX.PRT	This field is closely connected to the reaction classification "Chemical behaviour". It indicates that the reaction conditions (solvent, temperature, pH-value) refer to the prototype reaction of a series of experiments. Further variations of the reaction conditions are entered in this field.
Reactant AN	/RX.RAN	Accession Number(s) of reactant(s)
Reactant	/RX.RGT	Chemical name(s) of reactants(s)
Reaction Details ID	/RX.RID	Numerical
Number of Stages Stage Number	/RX.SRN /RX.STG	Number of stages in case of a multistep reaction. **Reaction stage**: a set of one or more (possibly experimentally inseparable) reaction steps leading to and/or from a detectable or presumed reaction intermediate.
Number of Steps	/RX.STP	Number of steps. **Reaction step**: an elementary reaction, constituting one of the stages of a stepwise reaction in which a reaction intermediate (or, for the first step, the reactants) is converted into the next reaction intermediate (or, for the last step, the products) in the sequence of intermediates between reactants and products.
Solvent	/RX.SOL	Information on the solvent or the solvent mixture used in the reaction. If a compound acts simultaneously as a reactant and a solvent, it is entered as a reactant, and not as a solvent.
Stage Reactant AN	/RX.SRAN	Accession Number(s) of stage reactant(s)

Stage Reactant	/RX.SRCT	Chemical name(s) of stage reactant(s)
Subject Studied	/RX.SUBJ	Present for the reaction classification "Chemical behaviour". Contains attributes like kinetics or product distribution.
Temperature	/RX.T	Temperature at which the reaction took place, numerical
Time	/RX.TIM	Time taken for the reaction
Reaction Type	/RX.TYP	Contains information on the reaction types assigned to a reaction, e.g. alkylation or name reactions such as Mannich Reaction.
Yield Data	/RX.YDT	Chemical yield (free text)
Yield Numerical	/RX.YDN	numerical
Yield (Optical)	/RX.YDO	Optical yield
Yield (Product)	/RX.YPRO	Chemical name(s) of the product for which the yield is given
Reactant AN (from detail)	/RX.RCAN	Reactant AN(s) for a specific detail, e.g. a "nonmapped reaction"
Product AN (from detail)	/RX.PRAN	Product AN(s) for a specific detail, e.g. a "nonmapped reaction"
Catalyst AN	/RX.CAAN	Accession Number(s) of catalyst(s)
Solvent AN	/RX.SOLAN	Accession Number(s) of solvent(s)
Record Type	/RX.RTYP	Keywords like "no reaction scheme"
Number of References	/RX.NUMREF	Numerical; recommended to evaluate before DISPLAY ALLREF for a specific reaction (displays might be lengthy).
Example Label	/RX.LB	e.g. "fig.1" shows the reaction, mostly refers to graphics or tables
Fulltext of Reaction	/RX.TXT	Example text
Example Title	/RX.TI	Title of the example, e.g. "proline ethylamide"
Location in Patent	/RX.LCN	location of a specific reaction in the patent document, e.g. "example 8a" contains the given reaction.
Reaction Structure Keywords	/RX.SKW	Keywords like "failed mapping" , "zero reaction"; related to structure
Number of Bond Changes	/RX.NBC	For display only, no search field
Preparation Reactants	/RX.BLB	PAN and RAN for a preparation (overall)
Reaction Reactant(s)	/RX.BLC	PAN and RAN for a reaction (overall)
Multistep details	/RX.MTEXT	Details like: "1.) methylal, ultrason, reflux then 1 h rt, 2.) reflux, 21 h, 2: 94 percent / 2N aq. NaOH / dioxane / 1.5 h"