

Experiment 28

Chemical Literature: Searching and Accessing Academic Publications

Often, you will need to access the chemical literature to find reference spectra for your compounds. More common molecules may be available in databases like SDBS, but the more complicated or rare your target molecule is, the less likely it is to be found there. Instead, you will need to access the original paper in which the compound was first reported in order to compare your spectrum to the literature.

There is no prelab or quiz for this experiment, but you can save some time by setting up a SciFinder account before the lab. To do this, go to www.orgchemboulder.com/Labs/Software and follow the instructions linked from there. This may take a few days, so request it well in advance of the due date.

The required parts of this experiment are marked with “Exercise.” For these parts, you should write up the results into a Word document, due in one week.

CAS Registry Numbers

The CAS Registry Number is an identification code assigned by CAS (the Chemical Abstract Service) to a unique substance when it is added to the CAS registry system. You can think of a registry number as a social security number for a chemical. Although each compound only has one CAS number, it can have many names. The molecular formula for a compound is not as useful in its identification, since there are many substances with the same molecular formula. For instance, there are 171 substances with the formula C₄H₈! However, only one registry number exists for each substance. Chemists have come to depend on the CAS registry number system for the absolute name, or identification, of a compound. The registry number is split into three groups of numbers, in the format XXXXXX-XX-X. The first segment can be two to six digits in length, while the second segment is always two and the last is always just one.

CAS Registry numbers are extremely helpful when you are looking up information about a compound, or trying to order a compound from a vendor. The CAS number is not subject to misspelling or alternate names and therefore it is much quicker to search for a compound. This is true whether you are searching in SciFinder, a public or company database, or even Google.

Exercise 1: Choose any experiment that you will perform for the remainder of this semester. Look up the CAS numbers for each of the reagents.

Downloading Papers and Supplemental Material

The standard for citing references in chemistry is the ACS Style Guide, 3rd Ed, published by the American Chemical Society. The complete style guide can be viewed at pubs.acs.org/isbn/9780841239999, though the most relevant part is Ch. 14 – References. Each author should be listed by their last name followed by their first and middle initials. The standard format for journal article citations is:

Author, A. A.; Author, B. B.; Author, C. C. Title of Article. *Journal Abbreviation*. **Year**, *Volume*, Start Page-End Page.

For example, an article might be listed as:

Fenick, D. J.; Taatjes, D. J.; Koch, T. H. Doxoform and Daunoform: Anthracycline-Formaldehyde Conjugates Toxic to Resistant Tumor Cells. *J. Med. Chem.* **1997**, *40*, 2452-2461.

Citations given in a compressed format will frequently omit the title of the article, leading to:

Fenick, D. J.; Taatjes, D. J.; Koch, T. H. *J. Med. Chem.* **1997**, *40*, 2452-2461.

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If you are mentioning this paper in the text of an article, you might refer to the authors as “Fenick et al.” “Et al.” is an abbreviation for “et alia”, which means “and others”.

Each journal has a commonly-accepted abbreviation for its name that is used in citations. For instance, any article that appears in the Journal of the American Chemical Society will be cited as being from *J. Am. Chem. Soc.* (although many chemists refer verbally to this journal as “JACS”). Many of the procedures used in this course are based on papers published in the Journal of Chemical Education, or *J. Chem. Educ.* (often referred to verbally as “J Chem Ed”).

A database of journal abbreviations can be found at cassi.cas.org/. This website also contains links to the online homepages for various journals, so you might be able to access an article directly this way. If not, the simplest approach is simply to google the full name of the journal, then check for a citation or reference search box on the journal’s homepage. Any journals published by the ACS are available at pubs.acs.org. You will probably need to either access articles from on-campus, or use VPN to do so.

Reading a scientific journal article is not the same as reading a novel or newspaper article. Often, the information is too dense to comprehend on a single pass, and understanding one part of an article will require referring backwards or forwards to another part of the article. Also, much of the time you may not be interested in most of the article, but you may need to just pull out some specific information (for instance, how to perform a particular step in a synthesis). More thorough guides to reading scientific papers are given at <https://www.elsevier.com/connect/infographic-how-to-read-a-scientific-paper> and web.stanford.edu/~siegelr/readingsci.htm. These are a useful guide.

The format of organic chemistry papers can vary widely, but papers that report new compounds will usually contain procedures for synthesizing them in an Experimental Section, near the end of the paper. They will also contain spectral data for the compounds, either in condensed form within the paper itself, or as an actual picture of a spectrum. Since the format of chemical journals often limits how long a paper can be, spectra will often be included in supplemental material (Figure 28-1).

Eight peptides were prepared in our experiment, each of the four marker-labeled products was produced twice. The results are collected in Table 1. The two hexanoic acid pep-

or electrochemistry. The SPPS approach as described in here is very versatile. The peptide sequence can easily be changed by simply adding more or other amino acids and the marker molecules may be changed to design new target bioconjugates. The marker can be organometallic or organic as shown in this article. An interesting use of peptides with organometallic markers in cell biology has been described (12). We have also applied inorganic complexes as markers to a heptapeptide nuclear localization signal (H-Pro-Lys-Lys-Lys-Arg-Lys-Val-OH), where a nitrogen ligand is used and late transition metals (for example Cu^{II} or Zn^{II}) are added in situ (13).

**Table 1. Analytical Data
for the Marker-Pseudoneurotensin Derivatives**

Marker	Yield/mg	ESI-MS/(m/z)		Composition
		Exp	Calc	
Hexanoic acid	56 (96%)	859.7	858.6	[M + H] ⁺
Hexanoic acid	56 (96%)	859.8	858.6	[M + H] ⁺
Cobaltocenium	17 (23%)	975.7	975.5	[M-CF ₃ CO ₂] ⁺
Cobaltocenium	49 (66%)	975.7	975.5	[M-CF ₃ CO ₂] ⁺
Ferrocene	51 (77%)	973.7	972.5	[M + H] ⁺
Ferrocene	49 (74%)	973.6	972.5	[M + H] ⁺
Rhodamine B	53 (64%)	1185.9	1185.7	[M-CF ₃ CO ₂] ⁺
Rhodamine B	60 (72%)	1185.9	1185.7	[M-CF ₃ CO ₂] ⁺

Supplemental Material

Student spreadsheets, instructor notes, a list of chemicals and equipment, hazards and safety instructions, reactions schemes and mechanisms, and ESI-MS of the products are available in this issue of *JCE Online*.

Figure 28-1: An example of a paper with supplemental material.

The majority of journal articles published in the last few decades contain references to supporting or supplemental information. This means that not all of the information from the article is contained in the article itself, but is instead located in extra documents linked from the journal’s website. If this is the case, the paper will mention it near the end of the document.

Each journal has its own method of organizing supplemental material. If the journal is an ACS journal, you can access the material by going to the page for the article and clicking “Supporting info.” You will then be shown a list of all the additional files for that paper.

Exercise 2: Download the paper cited above (the one by Fenick et al.) and its supplemental material. In the paper itself, go to pages 7 and 8 and note that the experimental procedures (the synthetic steps for synthesizing each compound in the paper) are each listed in their own paragraph, in the Experimental Section.

Imagine you are working in a research group, and your PI (Principal Investigator – the professor in charge of your research group) wants you to reproduce the results from this paper. She has asked you how you are going to distinguish amorphous daunofom from crystalline daunofom. What do you tell her?

If you are following a procedure from a published article, the article will often contain a list of each compound’s NMR peaks. This appears in a highly compressed format. For instance, after the description of the reaction used to form it, a compound’s ¹H NMR spectrum might be given as:

δH (CDCl₃; 200 MHz): 7.40-7.33 (m, 1H, Ar-H), 7.14-7.08 (m, 2H, Ar-H), 5.14 (d, J 6.5, 2H, OH), 3.88 (s, 3H, OCH₃).

The first set of parentheses indicates that the sample was dissolved in CDCl₃ and placed in a 200 MHz instrument. After that, there is a list of numbers. Each number or range indicates the chemical shift of each of the peaks in the spectrum, in order of descending chemical shift. The set of parentheses after each number contains a letter or letters to indicate the splitting of a peak (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet; it is also possible to see things like dd for a doublet of doublets or b for broad), and the integral of the peak (how many Hs contribute to it). It is also common to see the author’s assignment of which part of the molecule that peak belongs to (for instance, Ar-H indicates an aromatic proton), and the coupling constant (for instance, the OH peak in the example above has a J constant of 6.5). Even if you are not following the synthesis from a particular paper, you can still search SciFinder for papers which mention your compound, as described below. These papers will often list a spectrum, especially if they contain a synthesis of the molecule.

Exercise 3: The first row of Table 3 in the supplemental information for Fenick et al. lists chemical shifts of daunorubicin in its free base form in CDCl₃. Convert this list of values to the format given above, including as much information as you can for each peak. Note that the top of the table says “Chemical Shifts for Protons at Positions (Patterns, J Coupling Constants)”, so any numbers in parentheses should be formatted the same as J-constants were formatted in the example above.

SciFinder

SciFinder is an extremely powerful tool for literature research. It allows you to search by numerous chemical identifiers such as name, but its most useful feature is a structure search that allows you to draw a compound and then search for it, or for similar structures. You can sort your results by type (papers that include a synthesis of the compound, papers that include spectral data of the compound, patents, documents in a particular language, etc.). You can also search for particular steps in a synthesis, or syntheses of a set number of steps. Instructions for getting access to SciFinder are posted at www.orgchemboulder.com/Labs/Software/.

When you log in to SciFinder, you will see a list of search options on the left side of the window. For now, try out the structure editor. Open it up and draw the structure shown below in Figure 28-2. If you prefer,

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you can draw a structure in ChemDraw, save it as a .mol file, and import it into the structure editor. This may be easier in future if you have already drawn the structure for a lab report.

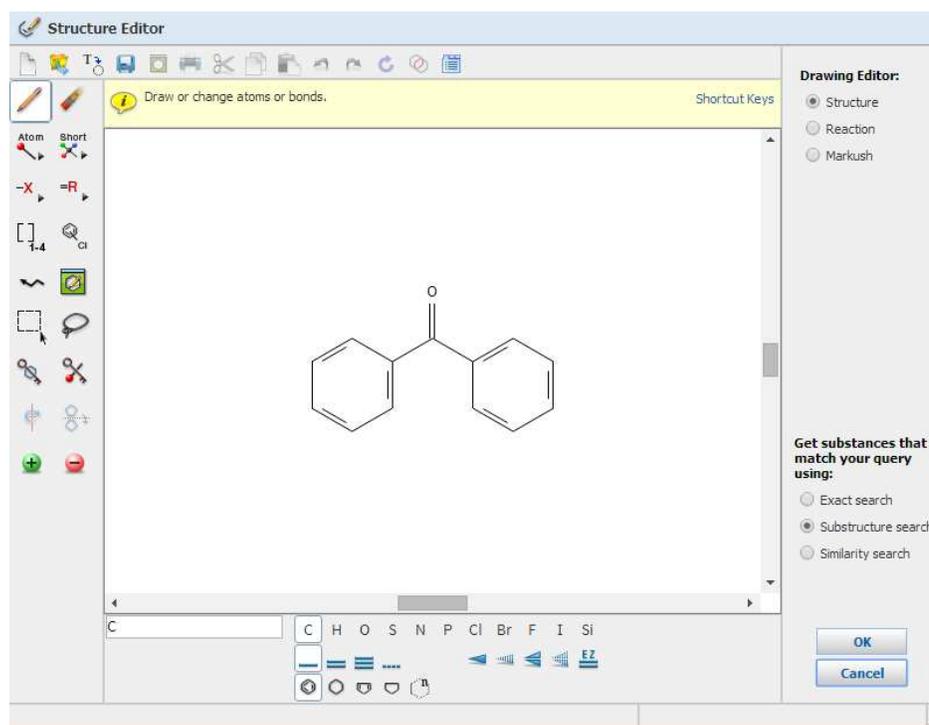


Figure 28-2: The Structure Editor window in SciFinder.

By default, “Substructure search” is selected in the bottom right. This means that SciFinder will search for any compounds that contain this group as part of a larger molecule. Click “OK,” then “Search,” and wait for the results. The results should be arranged in a grid, with the names, formulas and structures of each hit. Many of the structures will also have some icons around them, indicating what information is available: literature references, reactions that involve this compound, or companies offering this compound for sale. Below the structure, there may be links to spectra and experimental properties (Figure 28-3).

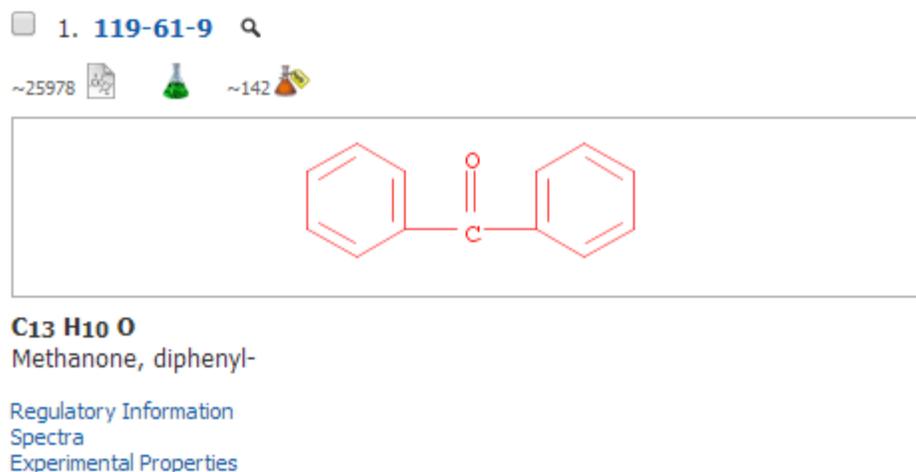


Figure 28-3: One example of a search hit in SciFinder.

For now, click the green flask icon; this will allow you find reactions involving this compound. Search for reactions where this compound is a product. You will see a list of results like those shown below in Figure

28-4.

1. View Reaction Detail  Link  Similar ReactionsSingle Step *Hover over any structure for more options.*

▼ Overview

Steps/Stages

1.1 R:Me-morpholineoxide, C:1555796-43-4, S:CH₂Cl₂, 80 min, rt

Notes

Reactants: 1, Reagents: 1, Catalysts: 1, Solvents: 1, Steps: 1, Stages: 1, Most stages in any one step: 1

References

Synthesis, spectral, electrochemical and catalytic properties of Ru(III) Schiff base complexes containing N, O donors

 Quick View  Full Text

By Raja, K. Kanmani et al

From Journal of Molecular Structure, 1060, 49-57; 2014

Figure 28-4: A reaction involving this compound, and a reference to the paper where it was published.

Each reaction should contain a reference to the paper where this result was published. If you wished to perform this reaction yourself, you could now go to the literature, get a copy of this paper, and follow the steps it contains.

Exercise 4: Perform a chemical structure search for any structure you like with at least ten carbon atoms, using the “substructure search” option. In your Word document, show the structure that you searched for and report how many results you got. If the structure you searched for has a CAS number, what is it?

The reaction structure search is even more useful, since you can look for particular functional group interconversions. It is similar to the chemical structure search, but you draw both the starting material and the product, and specify what role each one plays in the reaction (reactant, product, etc.) by using the button in the bottom left of the window that shows an arrow going from A to B. You can click this button then click each separate compound to describe it.

You can also label individual atoms to specify which atom in the starting material becomes which atom in the product. To do this, click the button in the bottom left that shows an arrow going from an atom labeled 1 to another atom labeled 1. Click an atom in one compound, then click the corresponding atom in the other compound (Figure 28-5).

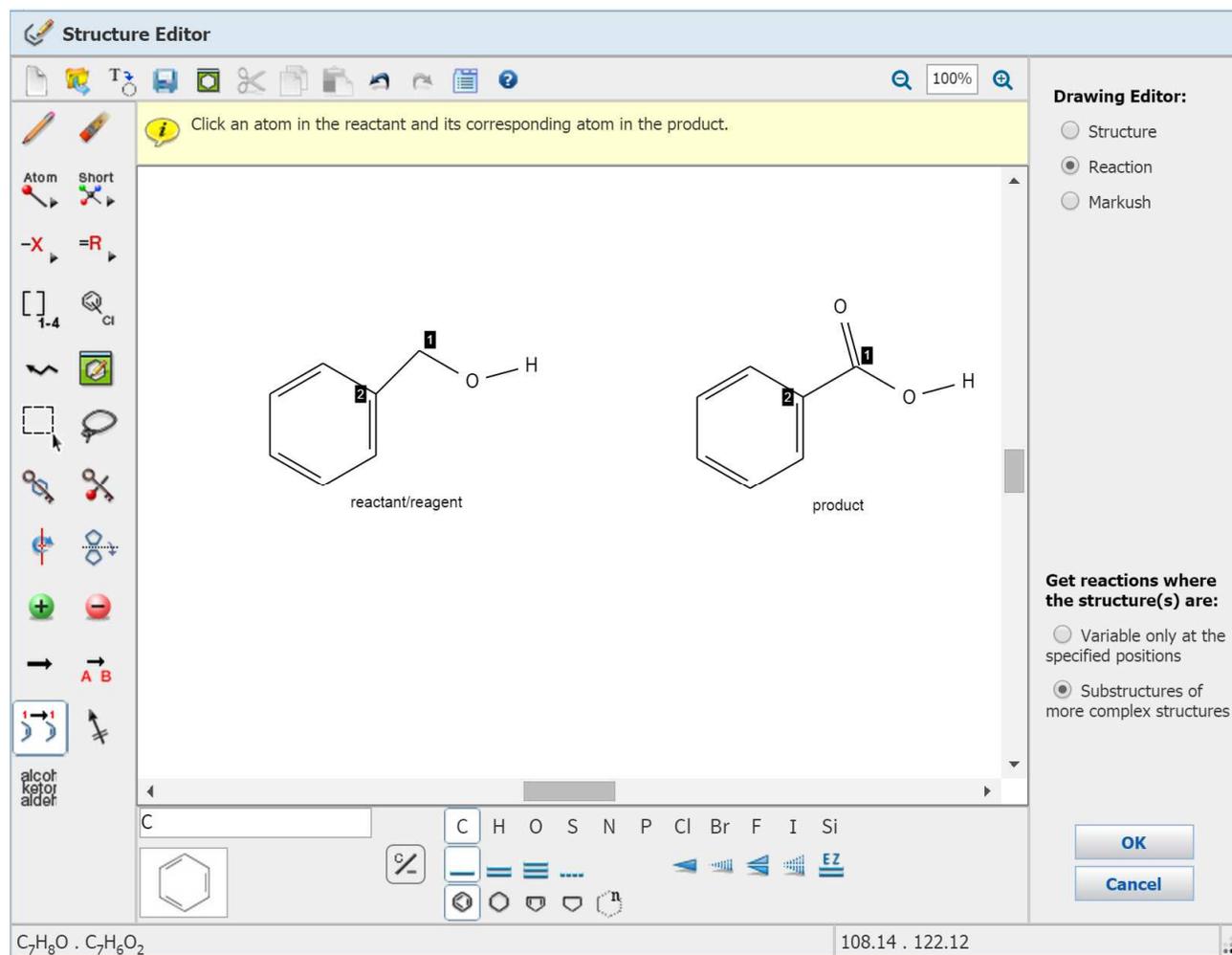


Figure 28-5: Using the Structure Editor to search for a reaction type.

Exercise 5: Return to the main menu and select “Reaction Structure”. Search for any functional group interconversion that you have covered so far in lecture, making sure that the atoms near the reaction site are numbered. In your Word document, show the reaction that you searched for and report how many results you got. For any one of the results, download the paper, provide an ACS-formatted citation for it, and copy the experimental procedure for the reaction that you searched for.