

Reversing the Elution Order in Chiral Chromatography Through the Application of Chiral Application Databasing

Version 8.0

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Introduction

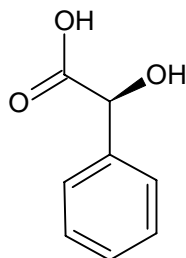
Using a chromatographic application database approach, it is possible to quickly find methods that have an excellent chance of eluting compounds in the opposite order. This process is similar to a standard application databasing approach, but incorporates searchability on the first/second eluted, which is information that is contained inside the user data fields in the [ChirBase™](#) [1] applications database. This approach is applicable whether your compounds are contained in the ChirBase database or not.

The Process

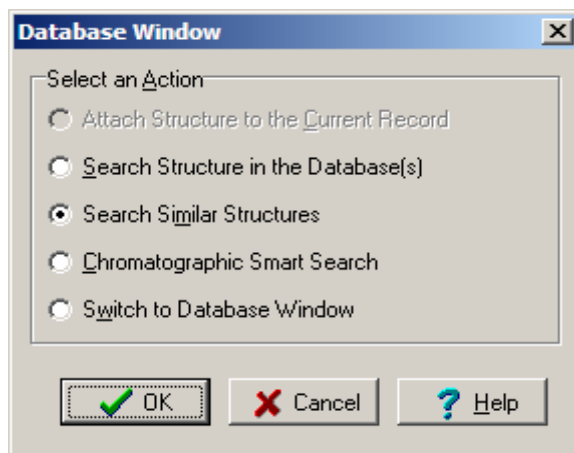
Step 1. Identify relevant compounds in the database.

The core search technique in [ACD/ChromManager](#) [2] is the structure similarity search. This search enables the researcher to find relevant compounds in seconds by ranking each compound in the database according to its similarity to the structure at hand. If the compound of choice is actually contained in the database, it will have a similarity of 1.0, regardless of the specific similarity search used. All other compounds are ranked between 0 and 1.0 based on shared functionality. The most common approach is to retrieve a method used for the most similar compound, and attempt it, or a method derived from it. This can greatly speed the process of development of new separations.

In the following example, we will search the ChirBase database for Mandelic Acid.



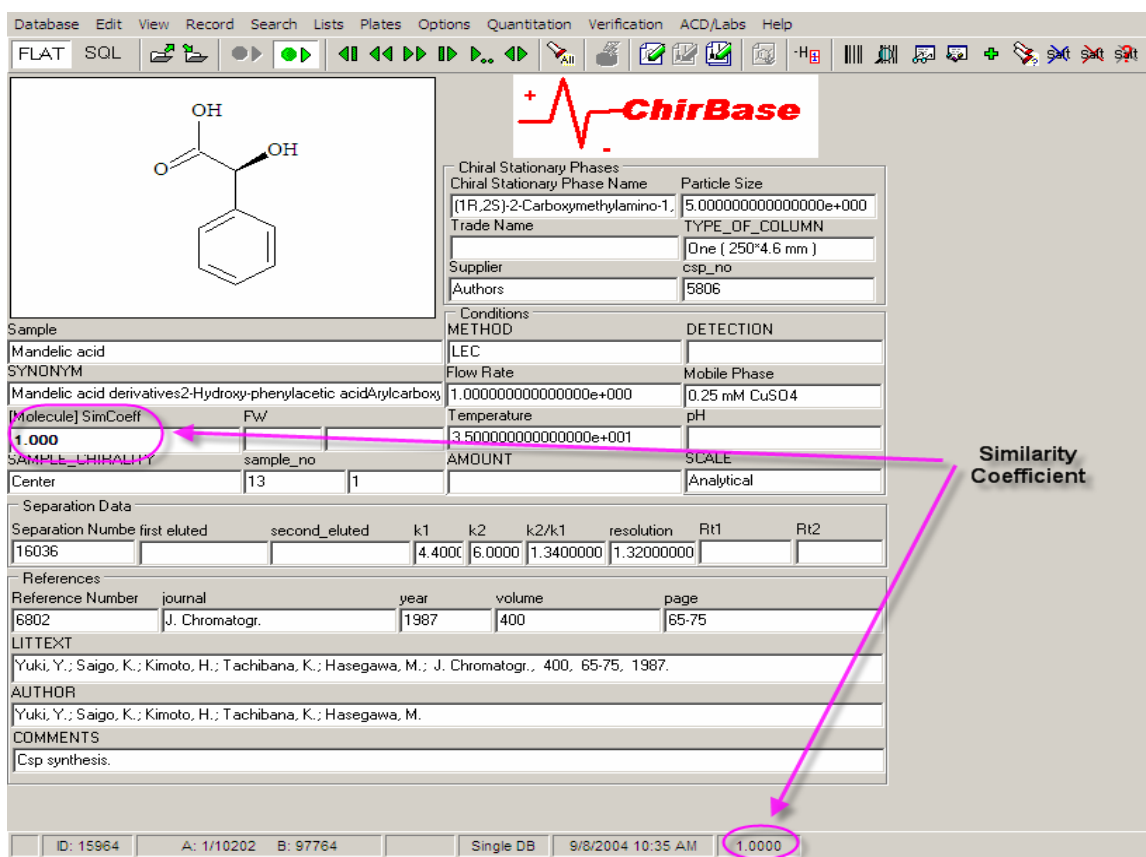
1. Draw the structure within [ACD/ChemSketch](#) [3], and then click the **Database** button on the bottom toolbar. You will see the Database action window:



2. Choose **Search Similar Structures**.

This gives 10202 hits in the ChirBase database for structures which have a similarity coefficient greater than 0.7.

Note The similarity search options are set within the Database window. Go to **Options > Similarity Search**. Here you can specify what type of similarity coefficient to use, and what criteria to display the hits.



Database Edit View Record Search Lists Plates Options Quantitation Verification ACD/Labs Help

FLAT SQL

O=C(O)[C@H](O)c1ccccc1

ChirBase

Chiral Stationary Phases	
Chiral Stationary Phase Name	Particle Size
(1R,2S)-2-Carboxymethylamino-1-	5.000000000000000e+000
Trade Name	TYPE_OF_COLUMN
	One (250*4.6 mm)
Supplier	csp_no
Authors	5806

Conditions	
METHOD	DETECTION
ILEC	
Flow Rate	Mobile Phase
1.000000000000000e+000	0.25 mM CuSO4
Temperature	pH
3.500000000000000e+001	
AMOUNT	SCALE
	Analytical

Sample	
Mandelic acid	
SYNONYM	
Mandelic acid derivatives2-Hydroxy-phenylacetic acidArylcarboxy	
Molecule] SimCoeff	Fw
1.000	
SAMPLE_CHIRALITY	sample_no
Center	13 1

Separation Data								
Separation Numbe	first eluted	second_eluted	k1	k2	k2/k1	resolution	Rt1	Rt2
16036			4.4000	6.0000	1.3400000	1.32000000		

References				
Reference Number	journal	year	volume	page
6802	J. Chromatogr.	1987	400	65-75

LITTEXT
Yuki, Y.; Saigo, K.; Kimoto, H.; Tachibana, K.; Hasegawa, M.; J. Chromatogr., 400, 65-75, 1987.

AUTHOR
Yuki, Y.; Saigo, K.; Kimoto, H.; Tachibana, K.; Hasegawa, M.

COMMENTS
Csp synthesis.

ID: 15964 A: 1/10202 B: 97764 Single DB 9/8/2004 10:35 AM **1.0000**

Step 2. View all applications for the same sample.

In some cases, the elution order found will not be the elution order of choice. The researcher may desire to find methods likely to reverse this order. In these cases, the researcher can take advantage of the fact that ChirBase often has multiple methods for the same compound available. If we return to the method that was retrieved, either for our compound or the related compound, we can quickly view all separations that were reported for that specific compound by right clicking on the compound in the database window, and choosing "**Search Current**". All applications for this exact structure will be shown.









Searching the database for exact structures now gives us 169 hits.

Step 3. Find any applications that reverse the elution order.

At this point, we need to find out if any of the applications reported the opposite elution order. The vast majority of ChirBase applications contain a report of observed elution order. If there are a small number of applications, the user can visually scan a table of values for first/second eluted to look for a reversal of order. Otherwise, a search can be performed for the opposite value. If a reversal of elution order for the sample is shown, this is likely to be a good candidate for the situation at hand.

It is possible to view the table of hits by changing the view to Table view. Go to **View** on the top menu, and choose **Table**. This will allow you to see the database in Table view from which you can visually scan the elution order using the first_eluted and second_eluted columns in the table.

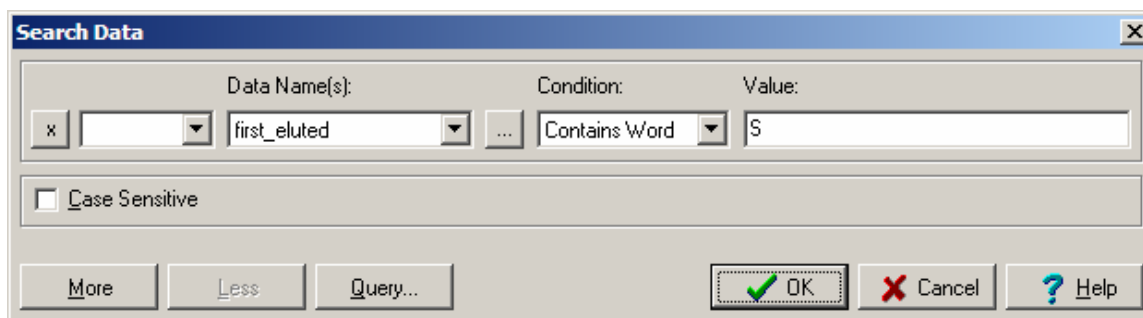
The database will contain five types of entry for the elution order: +/-, R/S, D/L, ?/?, and no value entered. There will also be combinations of these such as +R/-S etc.

#	#D	Structure	RXNREGNO	first_eluted	second_eluted	litref_no	REFERENCE...	AUTHOR	page
1	9		9	(?)	(?)	1	7531	Armstrong, D.W.; Han, Y.I.; Han, S.M.	275-281
2	505		505	(D)	(L)	1	6339	Fujimura, K.; Kitagawa, M.; Takayanagi, M.; Ando, T.	607-620
3	1191		1210	S-	R-	1	8385	Allenmark, S.; Andersson, S.	154-160
4	1983		2005	Elution order		1	7521	Okamoto, Y.; Aburatani, R.; Kaida, Y.; Hatada, K.	1125-1128
5	1985		2007	+L	-D	1	7521	Okamoto, Y.; Aburatani, R.; Kaida, Y.; Hatada, K.	1125-1128
6	1986		2008	+L	-D	1	7521	Okamoto, Y.; Aburatani, R.; Kaida, Y.; Hatada, K.	1125-1128
7	1987		2009	+L	-D	1	7521	Okamoto, Y.; Aburatani, R.; Kaida, Y.; Hatada, K.	1125-1128
8	1988		2010	+L	-D	1	7521	Okamoto, Y.; Aburatani, R.; Kaida, Y.; Hatada, K.	1125-1128

Another method of searching is using the Search criteria to search the User data fields. For example, in the hits we have, we may know that we want to search for all methods which show the S isomer as eluting first. To do this, go to **Search** on the top menu, and choose **"Record User Data"**.

Note For [SpecDB \[4\]](#) version 8.13 or earlier, this will be **Search> User Data**.

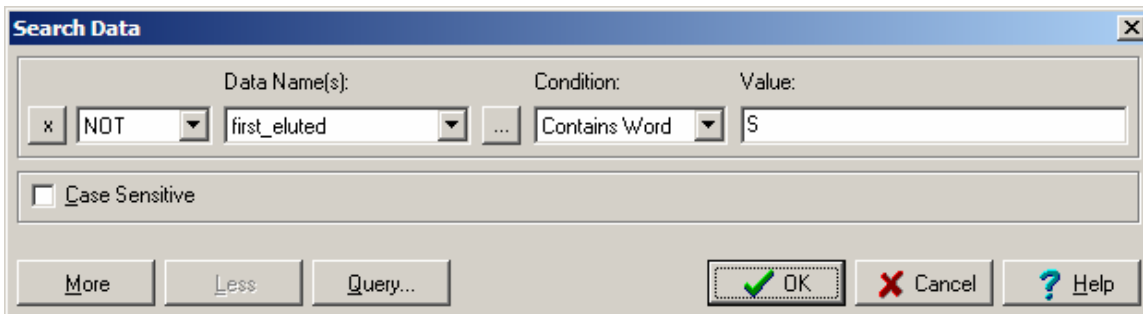
The Search Data window will appear:



Select the Data Name which you wish to find in the list of hits. In this case it is first_eluted, and the value S has to be present in some form in the first_eluted data field.

This finds 12 hits.

The alternative is to exclude all hits which have this specific elution order, for example we want to find all records which do not have S eluting first. Choose the NOT command as the operator, and leave the other conditions as before.



This would exclude all database entries which did not contain the word S as an entered value in the first_eluted data field. However, if a record does not contain a value for the first_eluted field, this search will not return this record as a hit.

This finds 45 hits.

Conclusion

Chiral applications databases provide a wealth of information on chiral separation behavior. By using the search and visualization capabilities of ACD/ChromManager in conjunction with ChirBase it is possible to quickly find the relevant selectivity for a given sample.

The extension of these capabilities can also be applied to find candidates for reversing the elution order of compounds. Choosing the elution order, and thus reversing the elution order, may be important for trace analyses or clinical studies, as well as preparative purification. For the preparation, or trace analysis of a given enantiomer, it is better that the required enantiomer elutes first.

References

1. ChirBase for ACD/Labs. http://www.acdlabs.com/products/chrom_lab/chirbase/chirbase.html/. February 15, 2005
2. ACD/ChromManager. <http://www.acdlabs.com/chrommanager/>. February 15, 2005
3. ACD/ChemSketch. <http://www.acdlabs.com/chemsketch/>. February 15, 2005
4. ACD/SpecDB. http://www.acdlabs.com/products/spec_lab/exp_spectra/specdb/. February 15, 2005