

An Automated Method for Verifying Structure-Spectral Consistency Based on Ion Thermochemistry

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Overview

We find that a large fraction of the major peaks in a mass spectrum can be rationalized using estimates of bond dissociation energies and a limited number of well-understood reaction paths. On this basis we have developed a computer method that links each peak in a mass spectrum to its most probable precursor fragment in a proposed chemical structure. It is designed to aid evaluators who now must manually perform these straightforward, but tedious tasks. It can also identify spectra in need of further evaluation. Unexplained peaks can indicate the presence of impurities, mass shifts or even an incorrect structure assignment.

This method has been developed for both radical cations and protonated molecules. While it is undergoing rapid development, it is now effectively treats a large fraction of C,H,O-radical cation fragmentation. It is routinely used for quality control of the NIST Mass Spectral Library.

Introduction

Well over 100,000 compounds are represented in comprehensive mass spectral libraries. This magnitude, along with the often complex relationship between chemical structure and mass spectrum, make quality control a very time-consuming (expensive) process that depends on the skills and patience of the evaluators. However, a large fraction of the peaks in the library arise from readily explained processes. Computer algorithms can 'pre-evaluate' such peaks to enable the evaluator to concentrate on the more difficult aspects of mass spectrum analysis.

Close examination of fragmentation 'rules' [1,2] shows that they can be reduced to a few general classes of reactions, relative rates of which depend on reaction thermochemistry. Since all spectra in the library are accompanied by computer structure representations, sufficient information is already present in the library for the application of these automated methods.

[1] "Mass Spectrometry of Organic Compounds", Budzikiewicz et al., Holden-Day, 1967

[2] "Interpretation of Mass Spectra, 4th Edition", McLafferty and Turecek, 1998

Thermochemical Kinetics

Relative abundances of ion fragments depend on relative dissociation rates of the precursor ion. "Thermochemical Kinetics", as developed by S.W. Benson, is used to estimate these relative rates on the basis of transition state theory, analogy and the principle of 'group additivity' [3].

This method has been widely used for reactions of neutral species and should be quite applicable to ion fragmentation kinetics for the following reasons:

-The most difficult-to-estimate property, intrinsic activation energies, is often negligible in ion reactions.

-Ion thermochemistry and structure are generally well understood.

-The fundamental reactions and transition states that underlie mechanisms of ion fragmentation are well known.

[3] "Thermochemical Kinetics, 2nd Ed", S.W. Benson, Wiley-Interscience, 1976.

Method

Assumptions

-Reactions rates follow statistical rate theory (transition state/RRKM theory)

-Only relative rates are significant

-Energy distributions can be ignored

-Reactions occur through electronic ground states

Bond Breaking

Estimates: Relative bond dissociation rates in an ion with sufficient energy to fragment depend primarily on relative bond strengths. We have developed a scheme for estimating these values based on values published in the NIST WebBook (webbook.nist.gov).

Chain and Ring Bonds: Fragments arise from rupture of non-ring (chain) bonds. When a ring bond is broken, new pathways for isomerization and dissociation usually become available.

Hydrogen transfer: H-transfer can occur in the last stage of a dissociation processes in competition with simple cleavage. These rates are hard to predict. When a labile H-atom is present in a newly formed ion fragment, its loss to the neutral fragment is simply assumed to be possible.

H-Transfer Isomerization

A variety of H-transfer rearrangements are treated, including those leading to double bond migration, 6-member ring transfer, transfer to oxygen/phosphorus and double H-transfer. Rates for each class are adjusted to match observations, with relative rates set up match estimated thermochemistry.

Multi-Step Processes

Several well characterized paths leading to dissociation are treated:

- gamma H-transfer shift induced dissociation
- double bond migration – can open up lower energy dissociation pathways
- ring-opening/H-transfer/dissociation sequences
- ring opening, beta-bond dissociation

Consecutive Reactions

Dissociation of weak bonds in un-rearranged products are allowed.

Unspecified losses of CH₄ and H₂O are also permitted.

Unspecified

A product ion that does not originate through a known path but whose m/z is consistent with the formal dissociation of two or three bonds is linked to the formal structure precursor. This usually indicates sequential decomposition processes. Also, all possible formulas are shown for any selected m/z.

Isotopic Peaks

All peaks in an isotopic cluster are grouped and theoretical relative abundances shown relative to the selected peak.

Fragmentation Summary

dissociation (simple, or with H loss/gain)

-gain only for selected processes

gamma H(or 2H)-shift dissociation

1,5-H-transfer in ring/dissociation

1,2-ring dissociation (Diels-Alder)

double bond migration/dissociation

selected special paths – e.g., H₂O loss

secondary beta-bond dissociation

secondary loss of CH₄ or H₂O

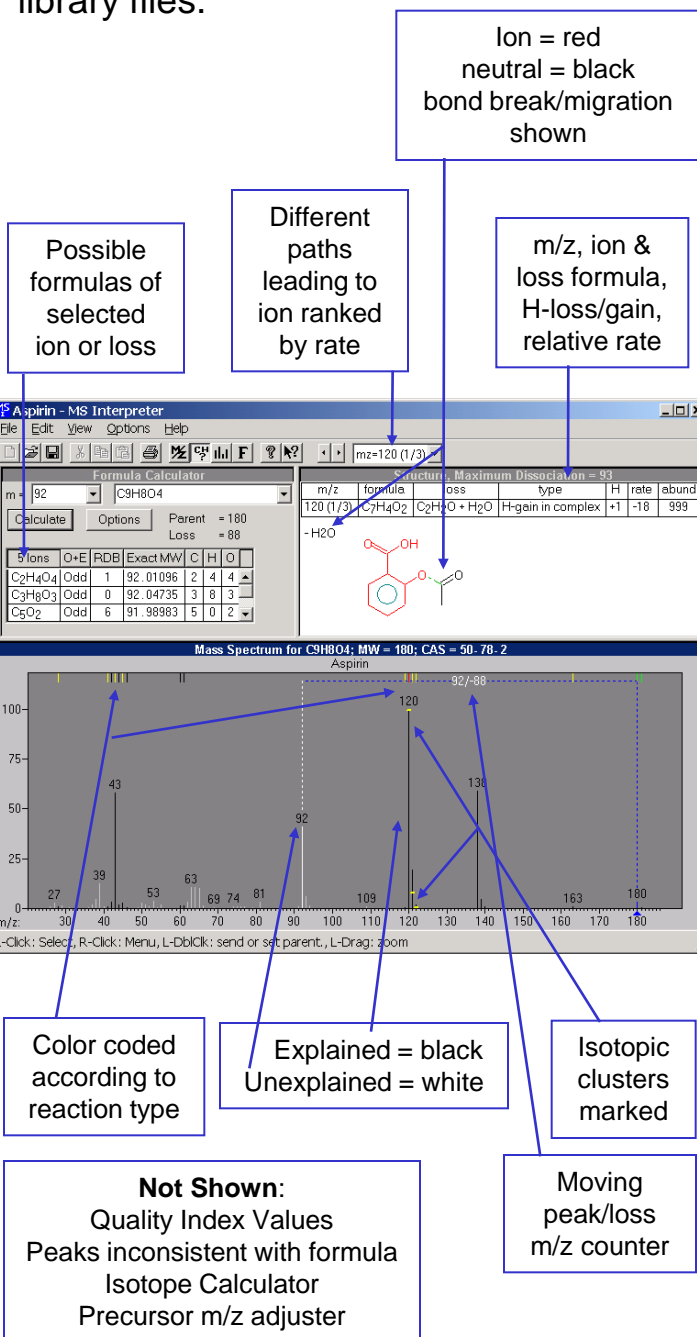
unspecified - 1,2 or 3 bond cleavage

- usually indicates a secondary process

Implementation

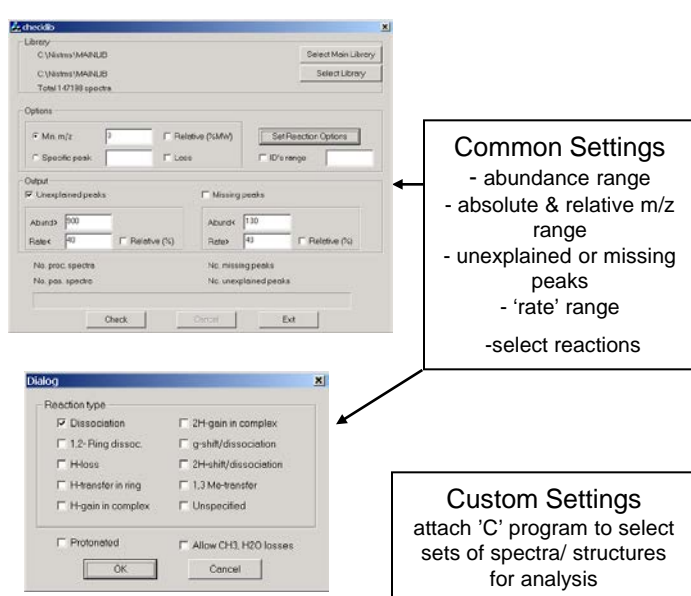
Spectrum Analyzer

'Unexplained' and 'Illogical' peaks are indicated; most probable origins of a selected peak is shown; integrated utilities for evaluation are included. Structure/spectra are taken from NIST library files.



Batch Analysis Program

Examines selected fragmentation paths for specified sets of spectra. Used to improve prediction of fragmentation, measure reliability and discover errors.



Future Work

-Incorporate all major fragmentation pathways [1,2] using thermochemistry as a constraint

-Fully extend to protonated molecules and anions

-Secondary reactions: re-submit each product ion to fragmentation logic

-Fine tune for error discovery and a 'spectrum quality index' (minimize false positive/negative peaks)

Availability

The first version of this spectrum evaluation tool is nearly complete and will be made freely available on the Web (chemdata.nist.gov).