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Short Research Article

# Some IT and data processing applications for $^{2}H$,$^{3}H$,$^{11}C$,$^{13}C$ and $^{14}C$-labelling†

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## Introduction

This paper describes three novel applications of information technology to isotopic labelling.

## Results and discussion

### Application 1: The Natural Abundance Isotope Correction program (NAIC)

This 1986 program[1a] has now been extended. The molecular ions of artificially labelled molecules have contributions to the peak intensities arising from both the isotopic labelling and from natural abundance heavy isotopes. NAIC[1a,1b] removes the latter, allowing determination of the separate contributions to the ion from each isotopomer, and hence the specific activity or isotopic abundance to be determined. As an example, Figures 1 and 2 show the NAIC output from the analysis of a 2:4:2:1 mixture of unlabelled, mono-, di- and tri-deuterated species.

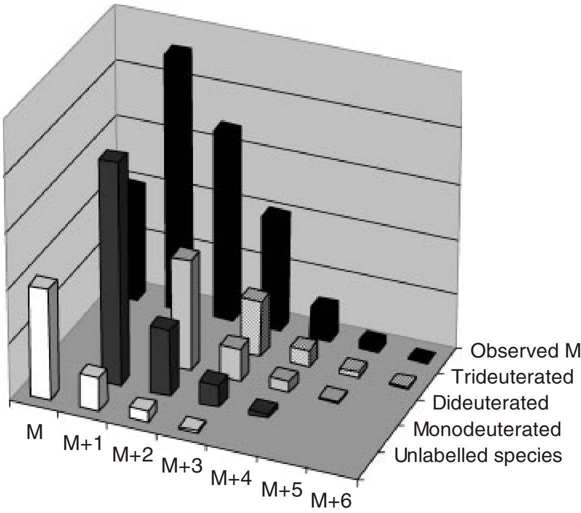

**Figure 1** Examples of NAIC-corrected data. The program can accommodate molecular ions from labelled compounds with masses up to 10 a.m.u above the unlabelled molecular ion. Data input requires the molecular ion intensities from the MS of the unlabelled compound or the molecular formula.

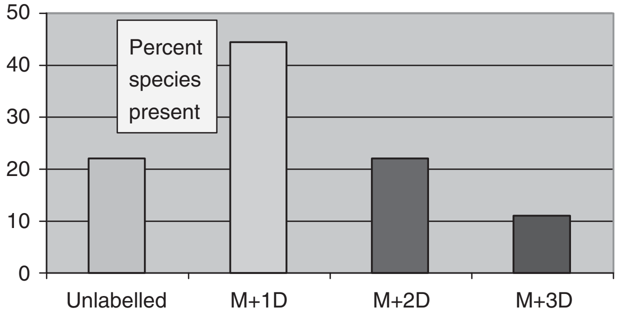

**Figure 2** Examples of NAIC-corrected data. The program can accommodate molecular ions from labelled compounds with masses up to 10 a.m.u above the unlabelled molecular ion. Data input requires the molecular ion intensities from the MS of the unlabelled compound or the molecular formula.

### Application 2: The Six-Site MS Modelling Program

This program models MS isotope clusters, providing abundance information on heavy isotopes at up to six molecular sites. Along with NAIC (above) it can correlate MS and NMR abundance data for $^{2}H$ and $^{13}C$-labelled compounds. Thus, heavy isotope labelling

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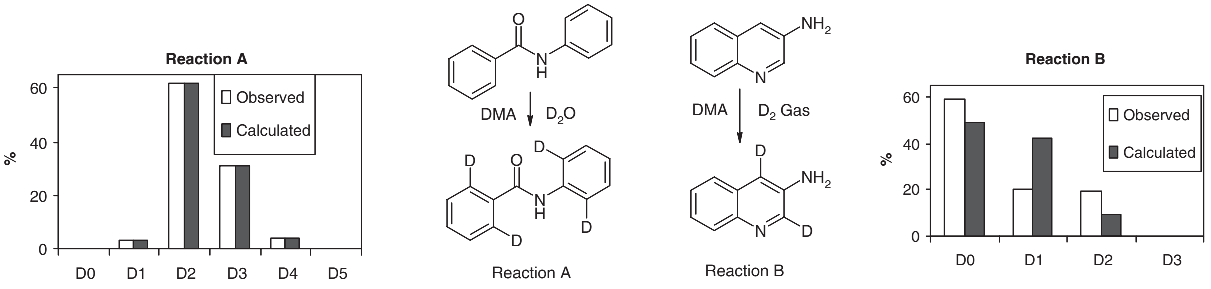
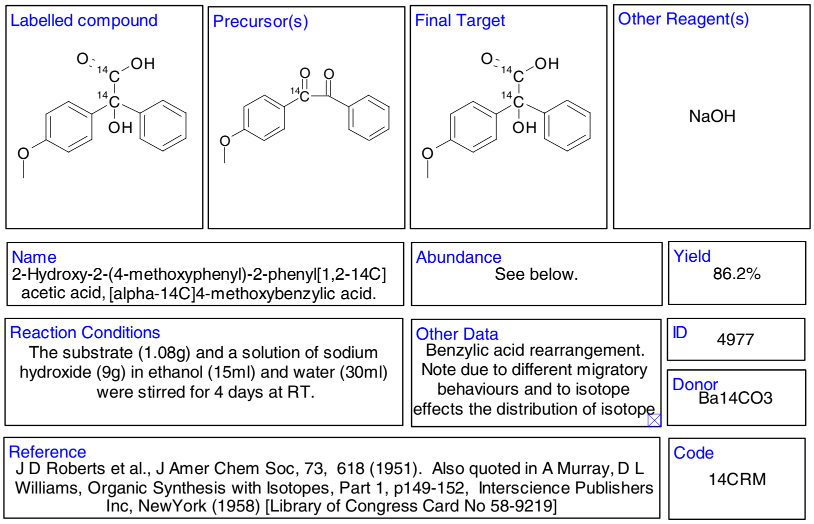


**Figure 3** Examples of statistical and non-statistical modelling by six-site MS.



Labelled compound

Precursor(s)

Final Target

Other Reagent(s)

NaOH

Name
2-Hydroxy-2-(4-methoxyphenyl)-2-phenyl[1,2-14C] acetic acid, [alpha-14C]4-methoxybenzylic acid.

Abundance
See below.

Yield
86.2%

Reaction Conditions
The substrate (1.08g) and a solution of sodium hydroxide (9g) in ethanol (15ml) and water (30ml) were stirred for 4 days at RT.

Other Data
Benzylic acid rearrangement. Note due to different migratory behaviours and to isotope effects the distribution of isotope

ID
4977

Donor
Ba14CO3

Reference
J D Roberts et al., J Amer Chem Soc, 73, 618 (1951). Also quoted in A Murray, D L Williams, Organic Synthesis with Isotopes, Part 1, p149-152, Interscience Publishers Inc, NewYork (1958) [Library of Congress Card No 58-9219]

Code
14CRM

**Figure 4** A typical record from the database.

(usually $^2H$ or $^3H$) may occur via a stoichiometric process (all molecules contain the same number of labelled atoms) or a more random process (a mixture of isotopomers with varying numbers of isotopic atoms). The six-site program allows this latter labelling to be statistically modelled.[2] Figure 3 shows the analyses of products from partial deuteration reactions carried out in the presence of $CODIrF_6Acac$.[3,4] Reaction A shows statistical labelling whilst reaction B does not.

## Application 3: The CoLogica© Labelled Compounds Database

Literature reviews of labelling with $^2H$, $^3H$, $^{11}C$, $^{13}C$ and $^{14}C$ are limited or outdated. Early accounts exist for $^{13}C$, $^{14}C$, $^3H$ and $^2H$, whilst the $^3H$-literature is currently under review. Although the major journals have indices, location of labelled compounds is laborious, especially syntheses prior to electronic journal submission. The CoLogica© Database contains thousands of records from a wide range of literature labelling reactions organised in areas of most interest to isotopic chemists. A typical record from the database is shown in Figure 4.

Sources such as local and international IIS symposia and major text books on isotopic synthesis (all omitted by the major search engines) are covered along with papers from major journals.

The database uses the MDL® IsisBase platform, and can be integrated with the in-house records of isotopic synthesis groups. The text fields are string searchable and the four structure fields are both structure and sub-structure searchable, including via isotope and isotope position.

## REFERENCES

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2. For $x$, $y$, $z$, etc., deuterium atoms at sites $a$, $b$, $c$, etc., the MS ion distribution may be modelled from the expansion of $(H_a+D_a)^x.(H_b+D_b)^y.(H_c+D_c)^z\ldots$, where $H_a$, $D_a$, etc.= fraction of isotope/site.

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4. Garman RN, Hickey MJ, Kingston LP, McAuley BM, Jones JR, Lockley WJS, Mather AN, Wilkinson DJ. *J Label Comp Radiopharm* 2005; **48**: 75–84.

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