

NMR yields

General

The ratio of compounds in a sample can be determined using the integrals of the peaks. Reliable integrals require:

- homogenous sample
- a homogeneous NMR sample
- sufficient relaxation time (d1) – **usually** not a problem in ^1H NMR, but in ^{19}F NMR we customarily extend d1 to 5 s
- absence of decoupling pulses (this is why the integrals in a standard ^{13}C NMR spectrum are not useful)
- good signal-to-noise ratio
- proper phasing of the spectrum
- absence of (significant) other contributions to the peaks chosen (*i.e.* the compounds being compared must have peaks that do not overlap with peaks from other compounds)

Assuming the conditions listed above, the ratio of the integrals give the ratio of nuclei, which need to be corrected for the number (N) of nuclei represented by the peaks chosen in order to give the molar ratio of the compounds:

$$(eq.1) \quad r_{A/B} = \frac{n_A}{n_B} = \frac{(\text{integral}_A/N_A)}{(\text{integral}_B/N_B)}$$

Not all peaks in the spectrum need to be free from overlapping peaks, but each compound to be determined must have at least one peak free of contributions from other compounds. It is preferable to chose simple peaks, as this makes it easier to see if there are overlapping impurities. However, the peaks chosen do not need to correspond to only equivalent nuclei – as long as there is no doubt about the number of nuclei represented by the peak chosen.

If a compound has several good (non-overlapping) peaks the average of the integral/N values can be used (alternatively, one may get a feeling for the precision of the method by observing the variation in the integral/N values for different peaks in the spectrum).

Yield determination with internal standard

When it is not feasible to identify and/or quantify all the components of a given mixture (*e.g.* a crude product) the amounts of specific (known) components may be determined by the use of an internal standard. The internal standard must be present in a known amount and its spectrum must have at least one peak that does not overlap with other peaks in the spectrum. The accuracy of the procedure is optimal when the integrations of the peaks are of similar magnitude, *i.e.* the amount of internal standard should be chosen judiciously.

The molar amount of analyte (A) can be calculated from the molar amount of internal standard (IS) and the molar ratio:

$$(eq.2) \quad n_A = n_{IS} \cdot r_{A/IS}$$

The mass of the sample does not factor into the calculation because the method relies solely on the molar ratio of the internal standard to the compound to be determined.

Yield determination without internal standard

When a sample consists only of known compounds, all of which have at least one clean peak for integration, the amounts of each compound can be determined. In this case the mass of the sample, as well as the molecular mass of each compound is needed. Water and traces of solvent may usually be ignored.

In this situation it is helpful to express the total mass of the sample as the sum of the masses of the components:

$$(eq.3) \quad m = \sum_{x=A, B, ..} m_x$$

Where m is the mass of the sample and m_x is the mass of component x in the mixture.

Inserting $m_x = n_x \cdot M_x$ into eq.3 we get:

$$(eq.4) \quad m = \sum_{x=A, B, ..} n_x \cdot M_x$$

Where n_x is the molar amount, and M_x is the molecular mass, of component x .

For a mixture of two components, A and B, eq.4 becomes:

$$(eq.5) \quad m = n_A \cdot M_A + n_B \cdot M_B$$

Inserting $n_A = n_B \cdot r_{A/B}$ into eq.5 gives:

$$(eq.6) \quad m = n_B \cdot r_{A/B} \cdot M_A + n_B \cdot M_B$$

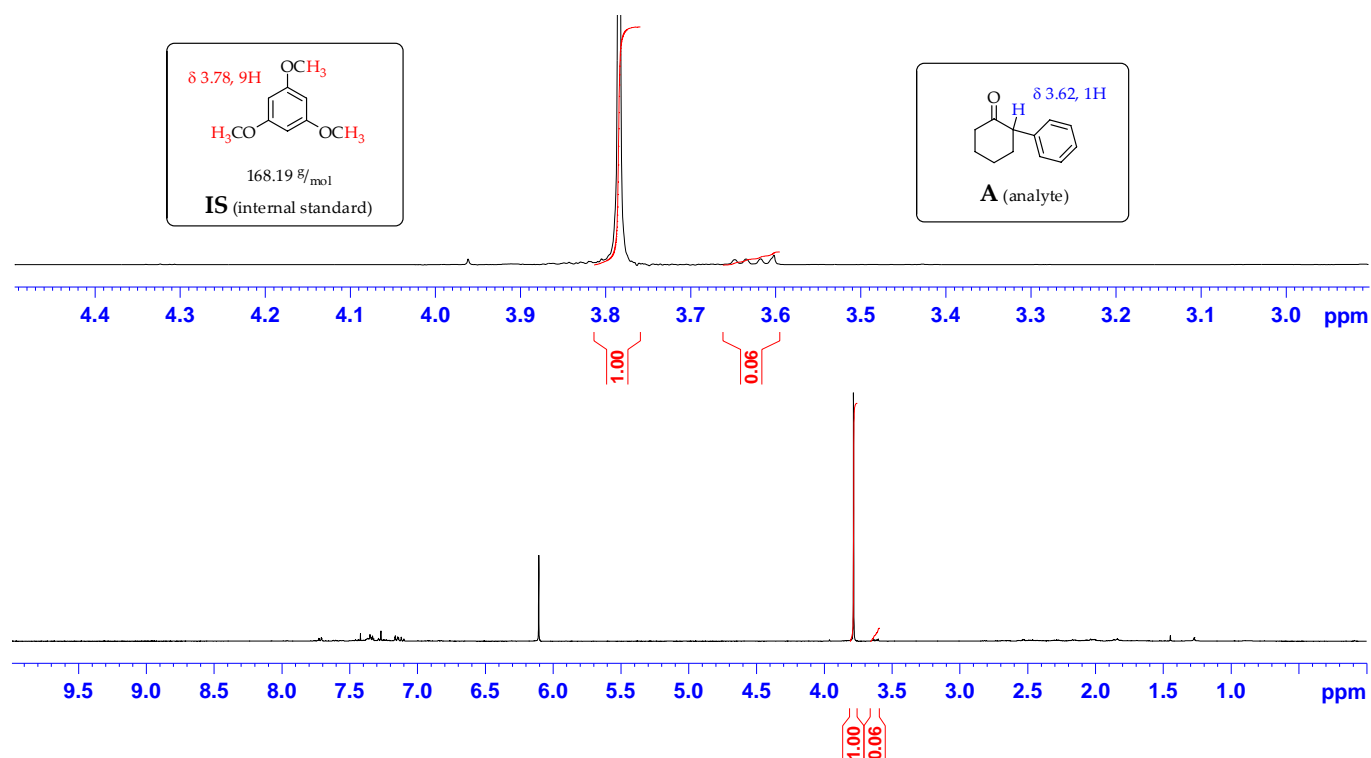
Solving eq.6 for n_B one gets:

$$(eq.7) \quad n_B = \frac{m}{M_B + M_A \cdot r_{A/B}}$$

Where n_B is the molar amount of material for (arbitrarily chosen) component B, m is the total mass of the mixture, and M are the molecular masses.

Once n_B has been determined this way, n_A can be determined via $n_A = n_B \cdot r_{A/B}$.

Example 1: Determination of the amount of 2-phenylcyclohexanone in a complex mixture with 1,3,5-trimethoxybenzene as internal standard:



The ratio between analyte and internal standard:

$$r_{A/IS} = \frac{0.06/1}{1.00/9} = 0.54$$

The sample contains 4.8 mg internal standard:

$$n_{IS} = \frac{4.8 \text{ mg}}{168.19 \text{ mg/mmol}} = 0.0285 \text{ mmol}$$

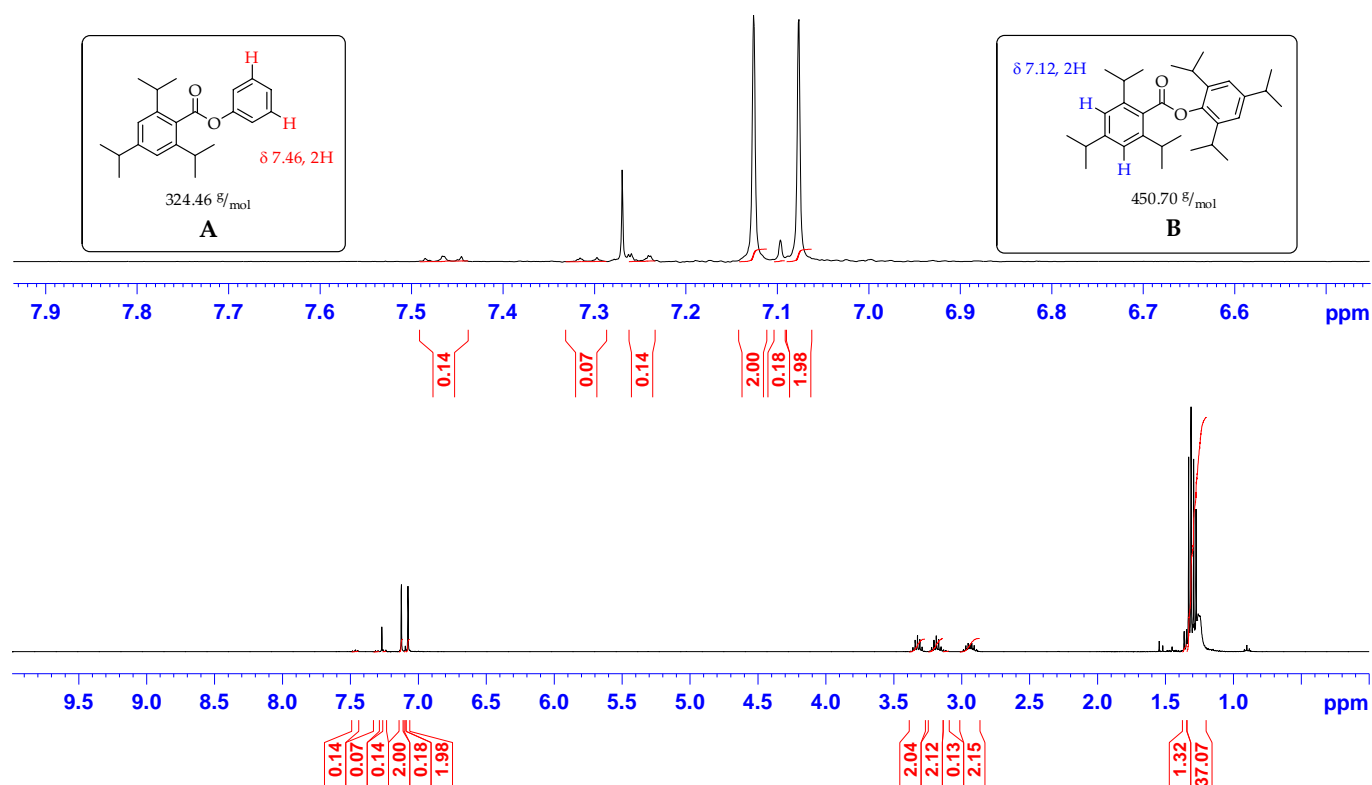
Inserting into eq.2 above gives:

$$n_A = 0.0285 \text{ mmol} \cdot 0.54 = 0.0154 \text{ mmol}$$

In this case the sample is a crude product of a reaction in which the theoretical yield of 2-phenylcyclohexanone is 0.25 mmol, therefore the NMR yield is $\frac{0.0154 \text{ mmol}}{0.25 \text{ mmol}} = 6\%$.

NB: in this case, the amount of internal standard has been chosen so that the integral of the product peak gives the NMR yield directly when the integral of the internal standard is normalised to 1.00. This is also intended to be in good agreement with the principle of comparing integrations of similar magnitude: For a 100% NMR yield the two peaks would have the same integration.

Example 2: Determination of the specific amounts in a mixture of (only) 2,4,6-triisopropylphenyl 2,4,6-triisopropylbenzoate and phenyl 2,4,6-triisopropylbenzoate:



The ratio between A and B:

$$r_{A/B} = \frac{0.14/2}{2.00/2} = 0.07$$

The mass of the mixture is 198 mg:

$$n_B = \frac{198 \text{ mg}}{450.70 \text{ mg/mmol} + (324.46 \text{ mg/mmol} \cdot 0.07)} = 0.418 \text{ mmol}$$

Using $n_A = n_B \cdot r_{A/B}$ gives:

$$n_A = 0.418 \text{ mmol} \cdot 0.07 = 0.029 \text{ mmol}$$

In this case the sample was obtained after column chromatography from a reaction in which the theoretical yield (of A and B) is 0.50 mmol.

Hence the NMR yields are...

$$\dots \text{A: } 0.029 \text{ mmol} / 0.500 \text{ mmol} = 6\%.$$

$$\dots \text{B: } 0.418 \text{ mmol} / 0.500 \text{ mmol} = 84\%.$$

Combined yield of A and B: 90%

The masses of the components in the mixture are easily obtained:

$$m_A = 0.029 \text{ mmol} \cdot 324.46 \text{ g/mol} = 9 \text{ mg}$$

$$m_B = 0.418 \text{ mmol} \cdot 450.70 \text{ g/mol} = 189 \text{ mg}$$