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Enhanced forensic discrimination of pollutants by position-specific isotope analysis using isotope ratio monitoring by ^{13}C nuclear magnetic resonance spectrometry

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ABSTRACT

In forensic environmental investigations the main issue concerns the inference of the original source of the pollutant for determining the liable party. Isotope measurements in geochemistry, combined with complimentary techniques for contaminant identification, have contributed significantly to source determination at polluted sites. In this work we have determined the intramolecular ^{13}C profiles of several molecules well-known as pollutants. By giving additional analytical parameters, position-specific isotope analysis performed by isotope ratio monitoring by ^{13}C nuclear magnetic resonance (irm-^{13}C NMR) spectrometry gives new information to help in answering the major question: what is the origin of the detected contaminant? We have shown that isotope profiling of the core of a molecule reveals both the raw materials and the process used in its manufacture. It also can reveal processes occurring between the contamination site 'source' and the sampling site. Thus, irm-^{13}C NMR is shown to be a very good complement to compound-specific isotope analysis currently performed by mass spectrometry for assessing polluted sites involving substantial spills of pollutant.

1. Introduction

Stable isotope analysis is now an established member of the set of tools used in forensics for traceability. Its key asset is the ability to distinguish chemically identical compounds coming from different sources. Stable isotope ratios, defined as the relative amounts of the heavy and light isotopes of an element in a given compound (e.g. $^{2}H/^{1}H$, $^{13}C/^{12}C$, $^{18}O/^{16}O$) can be measured with very high precision and can provide information about the geographical or botanical origin of the substance, or an insight into the chemical or biochemical pathway by which it was formed [1,2].

When applied to explosives or illicit drugs, the information obtained can be of significant value for Law Enforcement Agencies, at both strategic and tactical levels. First, a better understanding of the sources and migration paths of those products involved in terrorism and serious organized crime helps to tackle smuggling networks and hence improve the security of citizens. Secondly, evidence that several samples seized in different locations are from a common origin is useful information that aids field investigators and justice officers to combat illegal trafficking. In this respect, deducing the source can be the major issue for determining the liable party in forensic investigations of pollutants. The questions are then: (i) does the sample from a polluted site really originate from a suspected source? (ii) how similar or different are the samples taken? (iii) to what extent can we predict observed changes between the sample taken in the field and that from the suspected source due to known modifying processes? Several studies have shown that isotope compositional analysis can give some answers to these questions. Compound-Specific Isotope Analysis (CSIA) using isotope ratio monitoring by mass spectrometry (irm-MS) or by MultiCollector Inductively Coupled Plasma mass spectrometry (irm-MC-ICP-MS) has been proved to be an efficient method to trace and detect the origin of pollutants [3]. Determination of bulk isotopic composition (also known as 'mean', 'global' or 'total': the averaged contribution to the isotope value of all the atoms of a given element in the molecule under investigation) is mostly performed on ^{2}H, ^{13}C, ^{15}N, ^{18}O or ^{37}Cl depending on the nature of the studied pollutants [4].

Several studies have shown that the combined determination of ^{13}C and ^{37}Cl composition ($\delta^{13}C$ and $\delta^{37}Cl$) of chlorinated solvents such as trichloroethene (TCE) is able to distinguish samples provided by different manufacturers [5–11] and detect if TCE is the

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result of the degradation of tetrachloroethene [12]. Forensics studies using ^{13}C bulk isotopic composition have been carried out on methyl *tert*-butyl ether (MTBE) [13–15] and on monoaromatic hydrocarbons [3,16] or acetone [17] using ^{13}C and ^{2}H isotope analysis. Determination of ^{13}C and ^{2}H composition has also been performed on MTBE, toluene and/or heptane, using these compounds as tracers of the origin of gasoline [18–20]. Higher molecular weight structures, such as polyaromatic hydrocarbons (PAHs) and explosives, have been a target of environmental forensic studies [21–25]. Applications in the field have already been made and they have confirmed the potential of isotopic measurements to trace and detect pollutants [15,26].

However, the quality of the information gained from isotope analysis can be hampered by changes to the isotope ratios within compounds as they are involved in processes such as volatilization, sorption, hydrolysis, or bioremediation. Some effort has been made in forensics studies to take into account these changes in order to develop a more efficient tool to detect the origin of pollutants. Examples can be cited in which isotopic fractionation was induced by partial degradation [12,24], by partial evaporation of the plume, or by migration in soil [14]. These processes lead to a modification of the isotopic composition and make the determination of the origin more difficult [16].

In general, the larger the number of isotopic parameters measured, the more the information might be exploitable to relate the primary isotope compositions of the source and sample by better understanding the types of processes through which remediation has occurred. For example, when isotope ratios are used to determine quantitatively the proportional contribution of several sources to a mixture (such as the percentages of various sources in a groundwater plume), the use of n different isotope system tracers allows the proportional contributions of not more than $n+1$ different sources [27–29].

Two means can achieve this aim. The more currently used is multi-elemental isotope analysis, which gives information for each element present. The more recent development is Position-Specific Isotope Analysis (PSIA), which in principle allows the heavy isotope composition of each site of a molecule to be measured. Limited PSIA for $\delta^{13}C$ values ($\delta^{13}C_i$) can be accessed by irm-MS but only via complex and tedious (bio)chemical degradations [30] or through the on-line pyrolysis and GC separation of fragments coupled with mass spectrometry [31]. The latter methodology is, however, currently restricted to small molecules such as acetic acid, lactic acid or ethanol [32,33]. From a similar approach, PSIA of MTBE [34] and acetone [35] has been achieved, in which some position-specific values were obtained by deductive calculations. Isotope ratio monitoring by nuclear magnetic resonance spectrometry (irm-NMR) appears as a generic methodology for the determination of the isotope composition of each isotopomer: ^{2}H (irm-^{2}H NMR) [36] or ^{13}C (irm-^{13}C NMR). For the latter, it has been proved that new information is retrieved [37–41], and that this may be applied, for example, for tracking active pharmaceutical ingredients (API) or as a tool to detect patent infringements [42,43]. In such examples, irm-^{13}C NMR can be proposed as a means to track the target compound along the supply chain, especially by relating it isotopically to the starting materials [44].

In the environment, multiple processes can impact on the isotopic fractionation between source and sample. An important process is evaporation, and irm-^{13}C NMR has recently been applied to show that evaporation models could be considerably refined by exploiting position-specific ^{13}C fractionation [45]. The aim of the work presented in this communication is to demonstrate the potential of PSIA by irm-^{13}C NMR to characterize how the isotope profiles of several pollutants can be related to their sources. The work provides a comparison with results obtained from irm-MS and highlights the new information retrieved for tracing the source of contaminants or for discriminating chemical origin.

Table 1
Bulk ($\delta^{13}C_{bulk}$) and position-specific ^{13}C ($\delta^{13}C_{C-i}$) composition of each sample studied in this work, purchased from different origins. The sample code indicates the distinction between samples from the same origin but from different manufactured batches.

Compound[a]	Sample code	Origin[b]	$\delta^{13}C_{bulk}$ (‰)	$\delta^{13}C_{C-1}$ (‰)	$\delta^{13}C_{C-2}$ (‰)	$\delta^{13}C_{C-3}$ (‰)	$\delta^{13}C_{C-4}$ (‰)	$\delta^{13}C_{C-5}$ (‰)
MTBE	M1	Sigma-Aldrich	−28.9	−17.1	−40.5	−29.0	–	–
	M2	Sigma-Aldrich	−28.3	−15.6	−37.5	−29.5	–	–
	M3	Acros Organics	−27.6	−13.4	−41.1	−27.7	–	–
ETBE	E1	Sigma-Aldrich	−21.1	−11.6	−8.5	−31.4	−12.1	–
	E2	Sigma-Aldrich	−21.7	−12.1	−9.2	−32.1	−12.8	–
	E3	Alfa Aesar	−21.1	−10.9	−7.1	−32.2	−12.1	–
TAME	TA1	Sigma-Aldrich	−26.3	−16.0	−41.7	−24.1	−24.5	−26.8
	TA2	Sigma-Aldrich	−25.9	−13.4	−43.6	−22.9	−24.2	−26.9
TCE	TC1	Sigma-Aldrich	−30.7	−32.6	−28.8	–	–	–
	TC2	Prolabo	−35.0	−26.1	−43.9	–	–	–
	TC3	Acros Organics	−26.2	−25.5	−26.9	–	–	–
***n*-Heptane**	H1	Sigma-Aldrich	−28.9	−26.7	−35.3	−27.6	−29.1	–
	H2	Sigma-Aldrich	−41.9	−41.7	−51.1	−42.7	−36.7	–
Toluene	To1	Sigma-Aldrich	−23.1	−12.6	−23.9	−25.6	−25.4	−24.7
	To2	Sigma-Aldrich	−27.3	−22.2	−26.4	−28.3	−28.2	−31.4
	To3	VWR	−27.2	−22.6	−26.9	−27.3	−28.2	−30.9
Acetone	A1	Sigma-Aldrich	−30.6	−12.8	−39.4	–	–	–
	A2	Sigma-Aldrich	−24.7	−7.3	−33.4	–	–	–
	A3	Junsei Chemical	−6.4	12.7	−16.0	–	–	–

[a] MTBE: methyl *tert*-butyl ether; ETBE: ethyl *tert*-butyl ether; TAME: *tert*-amyl methyl ether; TCE: trichloroethene.
[b] All samples were bought in France, except sample A3 (acetone) obtained in Japan.

2. Material and methods

2.1. Chemicals

Samples of purity >95% were purchased from several manufacturers and/or from different batches (Table 1). DMSO-d_6, acetonitrile-d_3, dioxane-d_8 and acetone-d_6 were obtained from Eurisotop and tris(2,4-pentadionato)chromium(III) [CrAcac] from Merck.

2.2. irm-^{13}C NMR

Samples for quantitative ^{13}C NMR experiments were prepared as follows:

MTBE, ETBE and TAME: 500 μL+200 μL of 0.2 M CrAcac solution in acetonitrile-d_3;

TCE: 600 μL+100 μL of 0.1 M CrAcac solution in DMSO-d_6;

n-heptane: 500 μL+200 μL of 0.1 M CrAcac solution in dioxane-d_8;

toluene: 500 μL+200 μL of 0.2 M CrAcac solution in acetonitrile-d_3;

acetone: 500 μL+200 μL of 0.1 M CrAcac solution in DMSO-d_6.

Quantitative ^{13}C NMR spectra for all products, except acetone, were recorded using an AVANCE I 400 spectrometer (Bruker Biospin, Wissembourg, France), fitted with a 5 mm i.d. ^{1}H/^{13}C dual^{+} probe, carefully tuned at the recording frequency of 100.61 MHz. For acetone, an AVANCE III 400 NMR spectrometer connected to a 5 mm i.d. BBFO probe tuned at the recording frequency of 100.62 MHz, was used for obtaining $\delta^{13}C_i$ values to calibrate the AVANCE I spectrometer, as recommended for molecules such as acetone showing large chemical shift ranges [46]. For both spectrometers, experimental parameters for spectral acquisition were: without tube rotation; probe temperature 303 K; 90° pulse; sampling period 1 s; inverse-gated decoupling with an adiabatic pulse with appropriate phase cycles to avoid NOE [47]. The offset of the decoupler was placed at the middle of the proton frequency range for each compound. The number of scans was adjusted to attain a signal-to-noise ratio (SNR) ≥ 1500. Isotope ^{13}C/^{12}C ratios were calculated from processed spectra by curve fitting as described previously [40,42]. Five spectra were recorded for each measurement: the δ values reported for each carbon are the mean of the five spectra.

2.3. irm-^{13}C – EA/MS

Bulk ^{13}C abundance ($\delta^{13}C_{bulk}$) was determined by irm-MS using an Integra2 spectrometer (Sercon Instruments, Crewe, UK) linked to a Sercon elemental analyser (EA). A defined mass of each compound was weighted into tin capsules (2 × 5 mm, Thermo Fisher scientific) using a 10^{-6} g precision balance (Ohaus Discovery DV215CD) to give approx. 0.4 mg of compound. Great care was taken to ensure that there was no leakage from the capsule: (i) during the weighing of the VOC molecule introduced into the tin-capsule, the sealed capsule was left on the balance for a short period to verify the stability of the mass. No change in mass indicated that the capsule was effectively sealed, and (ii) the percentage of carbon in the analyte was checked by the operator against the theoretical value and by comparing this value with that usually obtained on the working reference. This gives a check in relation to the intensity of the signal of the CO_2 ions. Values of δ^{13}C (‰) are expressed relative to the international reference (Vienna-Pee Dee Belemnite, V-PDB) using the relationship:

$$\delta^{13}C_{VPDB}(‰) = \left(\frac{R_{sample}}{R_{standard}} - 1\right) \times 1000$$

The instrument was calibrated for δ^{13}C using the international reference materials NBS-22 ($\delta^{13}C_{PDB} = -30.03‰$), SUCROSE-C6 ($\delta^{13}C_{PDB} = -10.80‰$), and IAEA-CH-7 PEF-1 ($\delta^{13}C_{PDB} = -32.15‰$) (IAEA, Vienna, Austria) and instrumental deviation followed via a laboratory standard of glutamic acid.

3. Results and discussion

The primary objective of the data presented in this communication is to reply to the question: “does PSIA improve the capability to distinguish between chemical species from different origins?” We have selected for study a series of compounds commonly found as pollutants in the environment (Table 1) and which have already been studied for forensic investigation by irm-MS (see Section 1). Attention has been focused on the potential added value of $\delta^{13}C_i$ determination in addition to $\delta^{13}C_{bulk}$. Our working hypothesis is that the isotope ratios present in the raw materials used for manufacturing the compound should be related, via the synthesis process used, to those in the product, thus leading to specific $\delta^{13}C_i$ values and a characteristic intramolecular ^{13}C profile for each batch or origin.

To achieve this requires a sufficiently high level of accuracy. For all the samples studied in the present work, the SNR was >1500 leading to a standard deviation (SD) of 0.3‰ for the repeatability. This value is very similar to the precision observed for irm-EA/MS [48]. As a result, when a change in the ^{13}C profile by 1.2‰ (2 × SD, at 95% confidence level) could be distinguished, classification between sources is then possible. This interpretation is strengthen by PSIA in which the experimental data brought by each $\delta^{13}C_i$ is reinforced by its relative value to the other positions in the analyte.

3.1. Fuel oxygenates (MTBE, ETBE and TAME)

Bulk isotopic compositions of these compounds are very close between batches (Table 1). So, based on their $\delta^{13}C_{bulk}$ obtained by the irm-MS approach it would not be possible to deduce whether or not they were originating from the same or different sources. However, position-specific isotopic compositions measured by irm-^{13}C NMR indicate that $\delta^{13}C_i$ values are significantly different (i.e. $\Delta\delta^{13}C_i \geq 1.2‰$) between each batch for the C−1 and C−2 positions (see Fig. 1 for carbon numbering), in MTBE and TAME, but only for C−2 in ETBE. These carbons are a priori markers for tracing these additives during a pollution. The precursor compounds involved in the manufacturing of these ethers are: isobutene+methanol for MTBE or isobutene+ethanol for ETBE, and isoamylene+methanol for TAME. An inspection of the individual $\delta^{13}C_i$ values gives information on the origin of each raw material used. Thus $\delta^{13}C_{C-2}$ values of MTBE and TAME, corresponding to the carbon added to isobutene during the reaction with methanol, suggest that the methanol used for the synthesis of these two compounds has been produced using natural methane which is very impoverished in ^{13}C [49]. In marked contrast, the results obtained for C−2 and C−4 in ETBE (Table 1) would indicate that the ethanol used in the synthesis has been produced by fermentation of a C_4 photosynthesis-metabolism-type plant, such as maize or sugar cane, with a typical relative ^{13}C distribution between the two sites [33,39,50], with $\delta^{13}C_{C-2}$ also being slightly ^{13}C-enriched by the chemical reaction on isobutene for making ETBE. The similarity of the chemical process used for manufacturing these batches for a given molecule is depicted in Fig. 2, in which the intramolecular profile is normalized from the bulk ^{13}C content, thus showing that the relative intramolecular profile is identical for a given molecule.

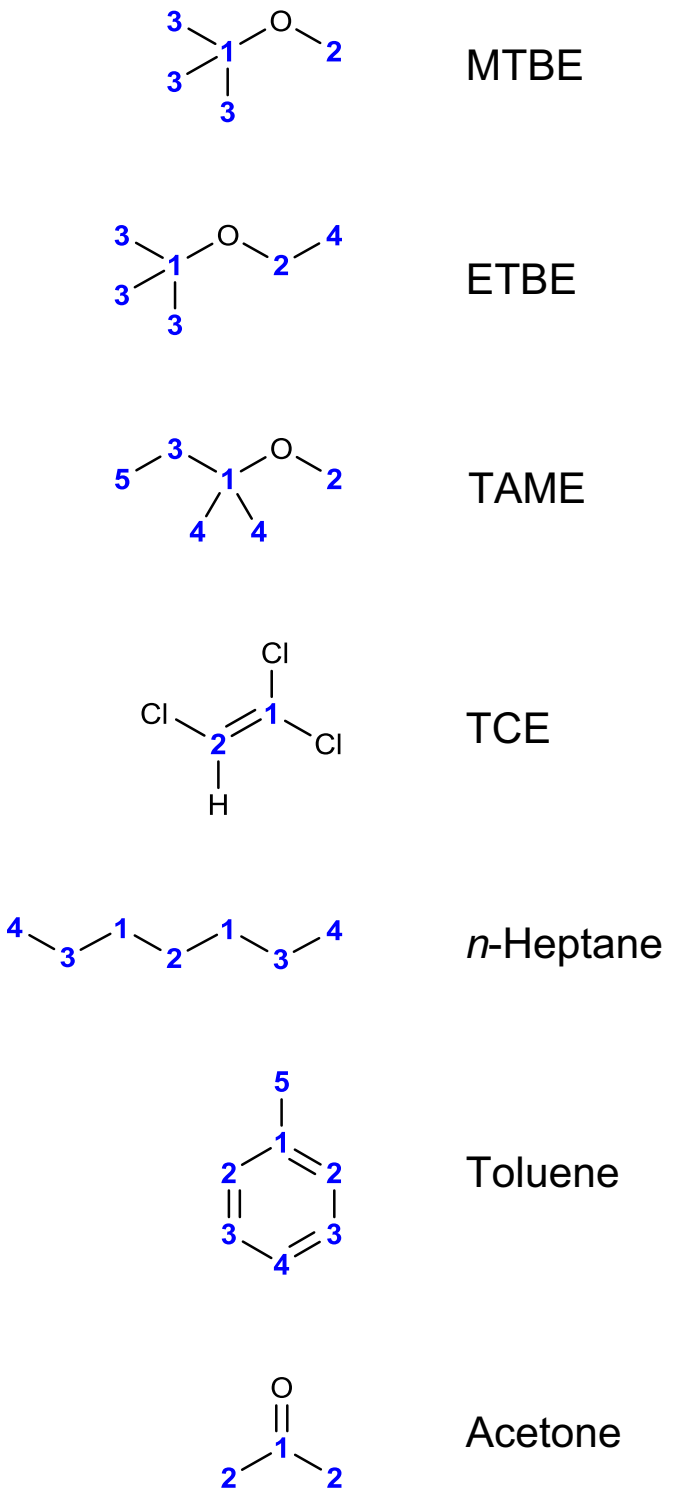

Fig. 1. The molecular structure of each compound with the carbon atoms numbered in relation to decreasing chemical shift in the ^{13}C NMR spectrum.

3.2. TCE

In the case of TCE, the bulk ^{13}C CSIA directly shows that the studied batches are from different origins. At a more refined level, PSIA indicates different ^{13}C distributions depending on the batch. The sample TC1 has $\delta^{13}C_{C-1} < \delta^{13}C_{C-2}$ whereas this is inverted for samples TC2 and TC3. The intramolecular profile confirms that the three batches are dissimilar with a real separation for TC1 (Fig. 2). The isotope discrepancy may be due to the process itself, in which the last step of chlorination could be fractionating.

3.3. n-Heptane and toluene

The results obtained on *n*-heptane batches show very different isotopic compositions both when the bulk and the PSIA are considered (Table 1, Fig. 2). No clear alternation of ^{13}C enriched and depleted positions along the carbon chain is apparent, as already found in *n*-alkanes shorter than C_{14} chain length [51]. These profiles (Table 1) are most probably the result of petroleum cracking and distillation during alkane production. The $\delta^{13}C_{bulk}$ of toluene samples would clearly suggest that batches To2 and To3 could be from the same origin and this deduction is strengthened by the PSIA obtained from irm-^{13}C NMR. Sample To1 has a higher bulk isotopic composition, which can be seen as due to the ^{13}C composition of C−1 and C−5 (Fig. 2).

3.4. Acetone

The three batches of acetone have very different $\delta^{13}C_{bulk}$ values, which is enough to distinguish them by CSIA. Analysis by irm-^{13}C NMR shows in addition that the carbon bearing the ketone function is consistently relatively enriched in ^{13}C, independent of the bulk value. This observation is not in agreement with the data obtained using irm-MS after decomposition of acetone [35]. The relative intramolecular ^{13}C profile accessible by irm-^{13}C NMR shows (Fig. 2) that the three samples are very similar, indicating that most probably they originate from the same process but using different sources of raw materials. Interestingly, the third sample, A3, which has a very different $^{13}C_{bulk}$ value is from Japan, a country in which a protocol using direct oxidation of propylene is commonly exploited [52]. The major producers in the world (mainly in the USA and Belgium) use the cumene process for synthesis [53], in which acetone is ensuing from the addition of benzene onto propylene with oxygen from air as oxidant and a radical initiator. In both cases, the carbon skeleton is provided by the propylene core and the central carbon is oxidized with, most likely, a similar isotope effect. Hence, it can be deduced that the differences between samples A1, A2 and A3 are due to the propylene source. Further experiments with isotopically defined raw materials are needed to confirm this.

4. Conclusion

The additional parameters retrieved from PSIA using irm-^{13}C NMR are potentially of considerable benefit for environmental forensic investigations in which the characterization of the source of pollution is of primary importance. The isotopic profiling of the core of a molecule reveals both the raw materials and the process used. Even when the molecules are relatively small, information can be gained on the similarity/dissimilarity between batches, as clearly demonstrated for MTBE, TCE or acetone.

The question that remains is “Can irm-^{13}C NMR be used on field samples and/or on dilute contaminants?”. It is clear that, compared with irm-GC/MS or even irm-EA/MS, NMR suffers from insensitivity and that therefore the amount required might not be available in a field sample However, it must be recognized that its limitation is not a matter of limit of quantification: rather, it is the extended analytical time required for measuring $\delta^{13}C_i$ on small quantities. Two current approaches can be envisaged to overcome this constraint. The first is instrumental: to improve the capability of making these measurements by NMR. There is an ongoing increase of sensitivity of NMR through (i) developing more efficient probes and (ii) by establishing new pulse sequences to increase sensitivity. Recent developments show that, even with a

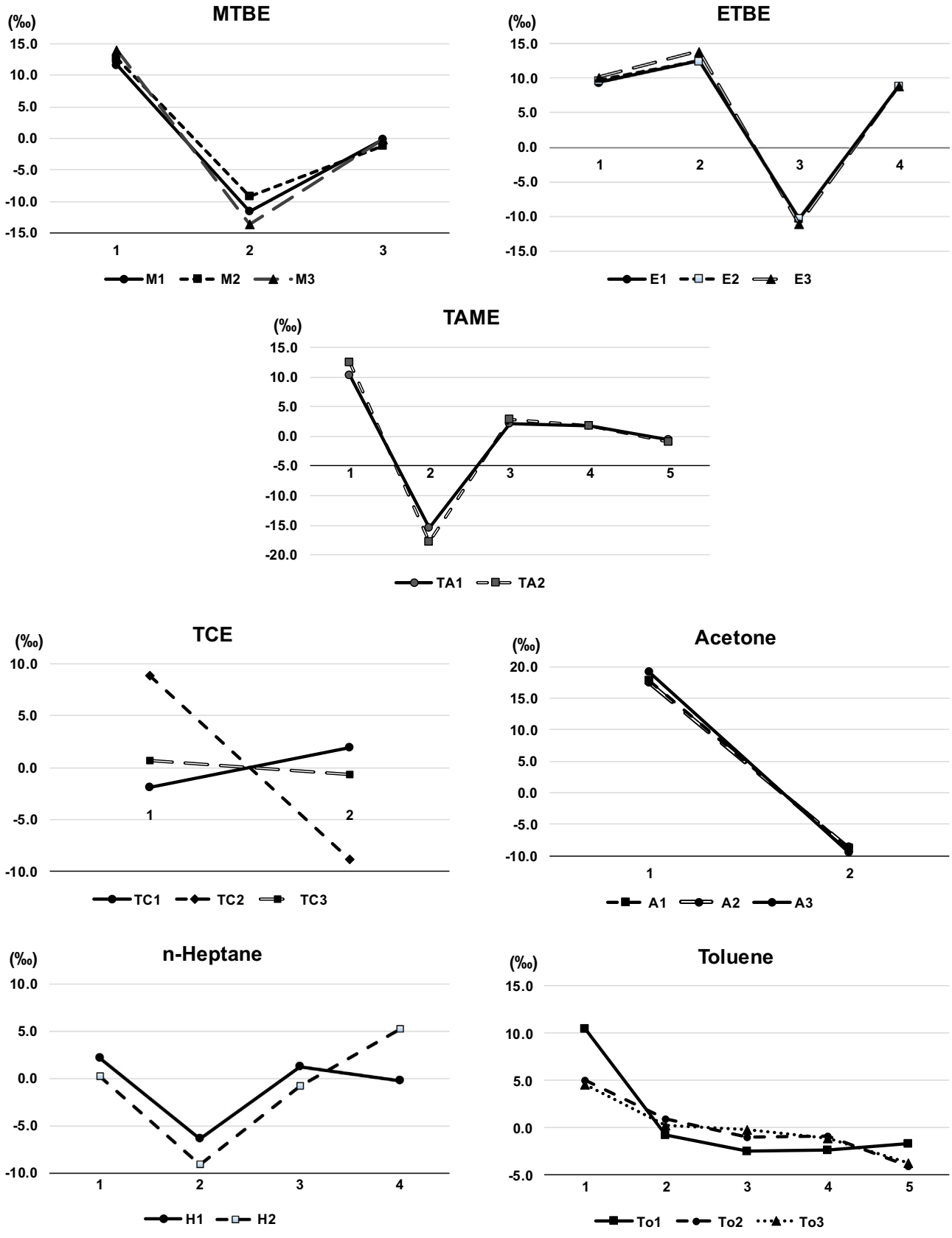

Fig. 2. Normalized relative isotope profiles of each batch for the molecules studied in the present work from the relation: $\Delta\delta^{13}C=(\delta^{13}C_i-\delta^{13}C_{bulk})$ as the *y*-axis in ‰. The figures on the *x*-axis indicate the carbon number for each molecule according to Fig. 1.

'moderate' magnetic field, (i.e. 9–12 T), a factor of 10–15 in sensitivity can be gained [43, 54]. Hence, the amount of sample required is reduced: instead of 400 mg of MTBE (as used in the present study), 30 mg would suffice. The second is in relation to the type and extent of the pollution and depends on the limit of solubility of each molecule studied in the present work. For the cases considered here, groundwater samples of 1–2 L of substantially contaminated water contain sufficient pollutant for analysis. The extraction/purification of the target molecule could be achieved by distillation, yielding appropriate amounts of sample (further details can be found in the supplementary information of Ref. [45]). Hence, even in its current configuration, irm-^{13}C NMR can be seen to provide a method that is adequate for field samples and as a good complement to existing isotope measurement techniques in environmental sciences.

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