Vacuum Electrolysis Reactor Technique for Quantitation of 13-Carbon Isotope Enrichment at the C1-Position of Formic Acid and Acetic Acid

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A specialized vacuum electrolysis reactor was designed, constructed, and utilized for 13-carbon isotope analysis of formic acid-^{13}C and acetic acid-^{13}C, each highly enriched at the C1-position. This reusable reactor was equipped with two platinum wire electrodes, miniature stir bar, and sidearm reaction chamber. The associated technique developed for 13-carbon isotope analysis is based upon electrolytic generation of carbon dioxide into the preevacuated reactor followed by gas inlet mass spectrometry. It proved practical to degas and electrolyze 95% formic acid (without added electrolyte) due to adequate ionic conductivity. Formic acid-^{13}C (nominally 99 at. % ^{13}C) was measured by electrolytic CO_2 generation to be 98.9 at. % ^{13}C. To analyze various ^{13}C-isotopic permutations of acetic acid, lithium and acid were separately added to reactor compartments, vacuum degassed, and stirred to produce an acidic solution. Thus, acetic acid-1-^{13}C that was nominally 99 at. % ^{13}C1 was determined by vacuum electrolysis to be 98.9 at. % ^{13}C1. Further, acetic acid-2-^{13}C that was isotope depleted at the C1-position (and known to be 99 at. % ^{13}C at C2) gave 0.8 at. % ^{13}C by mass spectrometry.

A variety of analytical technologies could be applied to measure 13-carbon isotope enrichment at the C1-position of small carboxylic acids. For example, the ^{1}H-atoms attached to the carbonyl carbon can be compared using magnetic resonance to estimate the 13-carbon enrichment of formic acid-^{13}C. Further, ^{1}H NMR could also be utilized to determine the 13-carbon enrichment at the C2-position of acetic acid since methyl hydrogen atoms are bonded to C2. It is problematic, however, to directly determine 13-carbon enrichment by ^{1}H NMR at the C1-position of acetic acid or propionic acid (that is, without chemical modification). Direct ^{13}C NMR measurements could be tried; however, such an approach is likely semiquantitative due to the nuclear Overhauser effect. In 1997, Brenna and co-workers reviewed position-specific isotope analysis (PSIA) by mass spectrometry including chemical, pyrolytic, and chromatographic approaches to isolate particular organic fragments.[1] Corso and Brenna also developed novel instrument systems to do on-line PSIA[1] of organics by combining pyrolytic

fragmentation, gas chromatography, and isotope ratio mass spectrometry.

A workable approach to measure ^{13}C-isotope enrichment at the C1-position of carboxylic acids is the site-selective generation of carbon dioxide. By strong chemical oxidation, it was shown possible to decarboxylate acetic acid using various catalysts, such as the following: pyrite or magnetite at 335 °C,[2] cobalt bromide/xylene at 95 °C,[3] or chromic anhydride/phosphoric acid at ≥30 °C.[4] It is also feasible to electrochemically generate CO_2 from carboxylate solutions. Indeed, it is documented that the Kolbe electrolysis[5] can produce carbon dioxide predominantly from the C1-position of small carboxylates such as acetate.[6–8] Historically the primary emphasis of the Kolbe process has been electrosynthesis of hydrocarbons by free radical coupling. Recently, Nonaka and co-workers fabricated a hydrophobic platinum electrode to electrolyze a series of aliphatic acids from acetic to octanoic.[9] The latter investigators distinguished between a "normal" product distribution of dimeric hydrocarbons (for cases such as acetate) and an "abnormal" distribution of alcohol, olefin, and ester products for longer chain carboxylates.

As the exclusive one-carbon carboxylic acid, formic acid is of particular interest for its possible use in fuel cells. Its electrooxidation in acidic solution has been intensively studied on platinum,[10,11] on sulfur-sorbed platinum,[12] and on platinum in an electrochemical pressure cell.[13] Under specific conditions, formic acid can exhibit current oscillations in response to electrooxidation.[14] Typically, decarboxylation of formic acid on platinum

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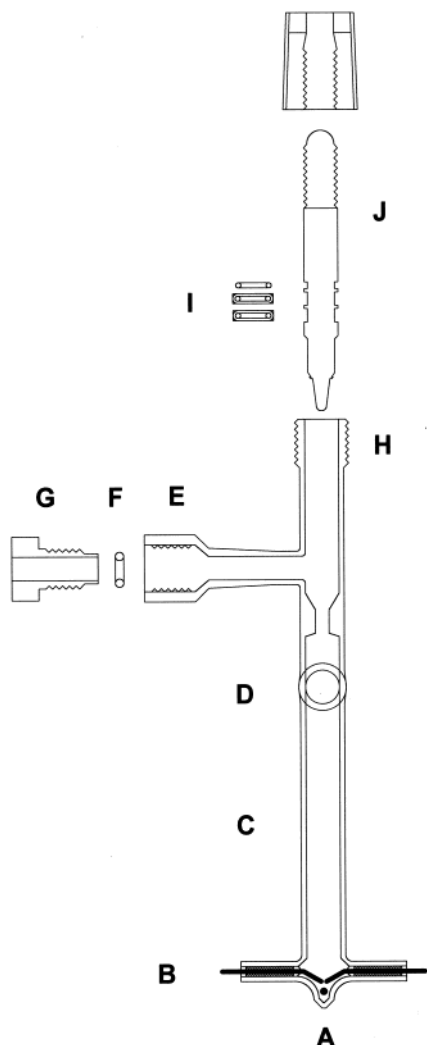
Figure 1. Exploded view of the core vacuum electrolysis reactor: (A) miniature magnetic stir bar, (B) platinum wire embedded in glass and solder, (C) glass body, (D) cross section of sidearm reaction chamber, (E) threaded port for tube, (F) O-ring, (G) PTFE bushing, (H) threaded valve port, (I) valve seals, and (J) reactor metering valve.
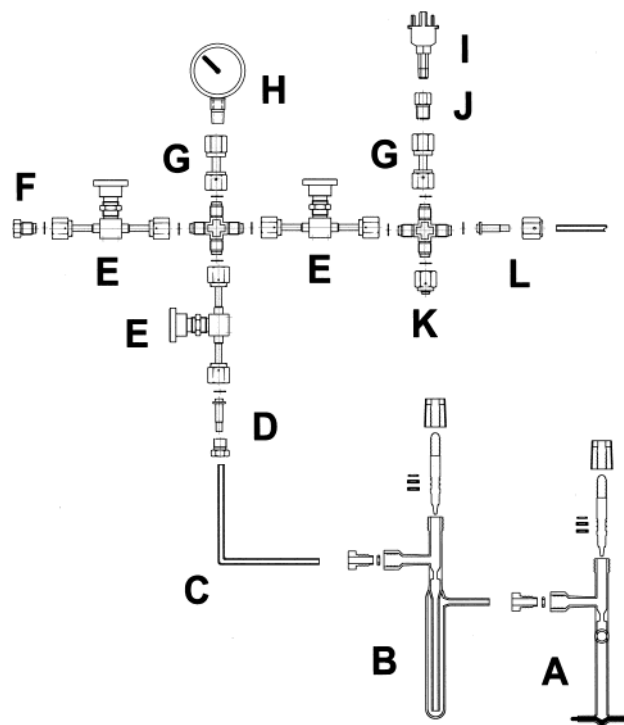

Figure 2. Exploded overview of the vacuum electrolysis reactor system: (A) reactor module, (B) glass-based condensation trap, (C) steel tube, (D) adapters tube to VCR, (E) bellows valve VCR, (F) plug-VCR, (G) adapters VCR to NPT, (H) bakeable pressure gauge, (I) thermal conductivity sensor, (J) steel bushing NPT, (K) cross-VCR and cap-VCR, and (L) adapters VCR to tube.

generates both carbon dioxide and carbon monoxide as products.

A key challenge to quantify 13-carbon isotope enrichment for any gaseous material is the avoidance of isotope dilution by 12-carbon during measurement. One viable technique to address this issue is to interface a gas control manifold to specialized chemical reactors. For instance methane-^{13}C and ethylene-$^{13}C_2$, each >99 at. % ^{13}C, were analyzed for 13-carbon isotope enrichment using a hermetic "spark combustion reactor".[15] Likewise, the present approach to measure ^{13}C1-enrichment of carboxylic acid began by designing a monolithic vacuum electrolysis reactor that is relatively gastight. In operation, the title module functions both as a solid−liquid batch reactor and electrolysis cell. The overall experimental system includes this portable batch reactor, a steel/glass/polymer gas control manifold, and a quadrupole mass spectrometer. Associated analytical methodology is convenient and applicable to ^{13}C1-enriched carboxylic acids such as formic and acetic.

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EXPERIMENTAL SECTION

Vacuum Electrolysis Reactor. An isometric section of the two-compartment reactor (internal volume ∼20 mL) is depicted in Figure 1. A sidearm reaction chamber (size ∼6 mL) was built-in to permit separate loading of liquid and solid reactants prior to degas and mixing operations. The reactor housing was constructed from 10-mm-i.d. borosilicate glass tubing. Two 1-mm-diameter platinum wires that function as electrodes were flame-sealed into circular glass ports. Electrode ends were adjusted to ∼1-mm spatial separation. Each platinum wire was also soldered to an external copper wire for electrical contact. A 2-mm PTFE-coated magnet was fitted for the electrolysis compartment to enable forced stirring. Dynamic vacuum was supplied to the reactor through one metering valve equipped with polymeric seals (Chemglass CG-562). The latter valve metered the gas flow through a threaded glass port (size 7, Ace Glass). This design made it easy to connect the reactor to rigid tubes by mechanical compression of a bushing/o-ring/tube assembly into the open reactor port (see Figure 2). To illustrate this feature, the vacuum electrolysis reactor was directly piped to the control manifold of a gas chromatograph with pulsed discharge helium ionization detection (GC-PDHID) for leak testing.

Gas Control Manifold. The gas control manifold utilized for electrolysis was built in-house for vacuum and pressure service. It is structurally based on 0.25-in. stainless steel modules having mostly VCR-type (all-metal) connections. Select manifold components are represented in Figure 2 as an exploded view drawing. Also shown in relation are the vacuum electrolysis reactor and its associated glass condensation trap. Construction of this

multipurpose manifold involved making mostly VCR connections as well as two NPT connections for sensors (NPT connectors were wrapped with PTFE tape). Excluding glass modules, the core manifold was successfully pressurized to 100 psig. A mechanical pressure gauge was installed that has desirable size, vacuum-pressure range, and upper temperature limit (McDaniel Controls KXO-HT, oxygen-cleaned steel). Figure 2 also shows a thermal conductivity sensor used to monitor milliTorr-level pressures (Teledyne Hastings, model VT-6). The 0.25-in. steel tube seen at upper right is ultimately connected to a rotary vacuum pump (Leybold-Trivac model D4B). By analogy to the reactor itself, it was straightforward to make reliable gastight attachments between manifold tubes and threaded glassware. Among the advantages of this VCR-based manifold, it was very convenient to simply detach select modules (glassware/gauges/sensors), seal the manifold, and then bake it out under vacuum. It should also be noted that the entire manifold system avoids any usage of grease.

Materials. Natural-abundance formic acid was used as received from Fluka (98% puriss grade, stabilized with water). Formic acid-^{13}C was prepared at Isotec from precursor that was >99 at. % ^{13}C, and it contained ~5% water. Natural-abundance acetic acid (chemical purity >99.7%) was used as received from Aldrich. Acetic acid-1-^{13}C, acetic acid-2-^{13}C, and acetic acid-$^{13}C_2$ were each synthesized at Isotec with a nominal isotopic enrichment of 99 at. % ^{13}C. The water content of each ^{13}C-enriched acetic acid was measured to be <0.1 mass % based upon Karl Fischer coulometric titration. Lithium hydroxide powder (>98%) was obtained from Aldrich. Lithium metal (99.4%, 1–6-mm granules) was obtained from Alfa-Aesar.

Instrumentation. An Extrel-QGP quadrupole mass spectrometer was used to determine isotope enrichments. Its steel-based gas inlet system with integrated turbopumping station was used to meter gas to the QGP source. This process-type mass spectrometer was equipped with open-source electron ionization at 100 eV, quadrupole mass filter (unit mass resolution), and electron multiplier detection. Multiple vacuum background and product mass scans were obtained at 10 amu/s and averaged for storage. Typically 10^{-7}–10^{-6} Torr of electrolysis gas was metered into the spectrometer for measurements.

To accomplish gas chromatographic testing, an Agilent-6890-GC was modified by Wasson-ECE for gas-phase 0.5-mL sample injection. It was equipped with a discharge helium ionization detector operated at 150 °C (Valco Instruments). A robust gas control manifold interfaced the GC-PDHID to gas sample containers. The analytical GC-column utilized was a 5-Å molecular sieve PLOT type (Chrompack, 0.53-mm i.d./25 m), and the GC system was externally calibrated with primary standards (Matheson Trigas).

Procedure. A summary of the analytical methodology follows. The clean vacuum electrolysis reactor is initially connected to the gas manifold (see Figure 2), opened to dynamic vacuum, and checked for any significant leak. Next it is loaded with a stir bar, known mass of liquid acid in the electrolysis chamber, and (if needed) known mass of solid reactant in the sidearm chamber. Lithium or lithium hydroxide was the reactant utilized for electrolysis of acetic acid or propionic acid, and the amount typically added was 5–10 mol %. For instance, a representative trial involved prereaction of 0.03 mol of acetic acid-1-^{13}C with 0.001

mol of lithium. Following attachment of the loaded reactor to manifold, the chemical system is gradually degassed through the partially open metering valve. By hand rotation of the reactor about its circular manifold port, the degassed reactants can mix in the sidearm chamber (with optional forced stirring). To avoid reactive overpressurization, a metered dynamic vacuum was maintained from the manifold during any vigorous gas evolution. Liquid–solid reaction was judged complete once the mix was visibly homogeneous.

The resultant acid–carboxylate solution was again vacuum degassed, and afterward the reactor was isolated by closure of its PTFE valve (**Caution**: take appropriate safety measures to shield the analyst during all vacuum and electrolysis operations). Next, electrolysis was carried out using a regulated dc power source (Extech model 382213) to supply the requisite energy. Generally, a constant dc voltage was applied to the reactor electrodes while monitoring current with a multimeter (electrolytic reaction range 5–100 mA). To limit maximum reactor pressure, the total charge supplied per electrolysis was usually capped near 50 C; this imposed condition kept the internal pressure below 2 atm absolute.

Following electrolysis, the closed reactor would be detached from the gas manifold and transferred to a sampling inlet of the detection instrument (here MS or GC). After evacuation to the mass spectrometer base pressure, multiple scans were collected from m/z 44 to 49 for both background and product. Thus, the spectrometric signal at each unit m/z ratio was averaged and background corrected for all isotopic calculations. The pH of select carboxylate solutions was also measured after electrolysis-MS using indicator strips (colorpHast, EM Science).

Estimation of 13-Carbon Isotope Enrichment. The isotope enrichment calculation was an improved modification of a previous computer algorithm.[15] Generally the ^{13}C-atom fraction was estimated by fitting the normalized mass spectrometric signals from m/z 44 to 49. Such fitting algorithms incorporated a weighted least-squares search[16] coded in Visual Basic (version 6.0, Microsoft). Alternately the ^{13}C-atom fraction could be roughly estimated by calculating the baseline-corrected spectrometric ratio of m/z 45 signal to m/z (44 + 45) signal.

RESULTS AND DISCUSSION

Consideration of select priorities helped guide the design of this two-compartment electrolytic reactor. These included mechanical reliability, compact reactor size, reactor reusability, avoidance of organic additives, and simplicity of operation. Each of these desirable outcomes was acceptably realized in practice. Since the vacuum electrolysis reactor is essentially monolithic, it has proven to be both robust and reusable. Internal reactor pressures ranging from vacuum (~10^{-2} Torr) to >1-atm absolute have been applied to it without noticeable damage. Another significant advantage is its small size (mass ~0.065 kg). The latter feature makes it easy to transport the reactor after electrolysis to a gas analyzer of choice. Other than gross breakage, one limitation of this present design is eventual vacuum failure due to deterioration of the glass–platinum seals.

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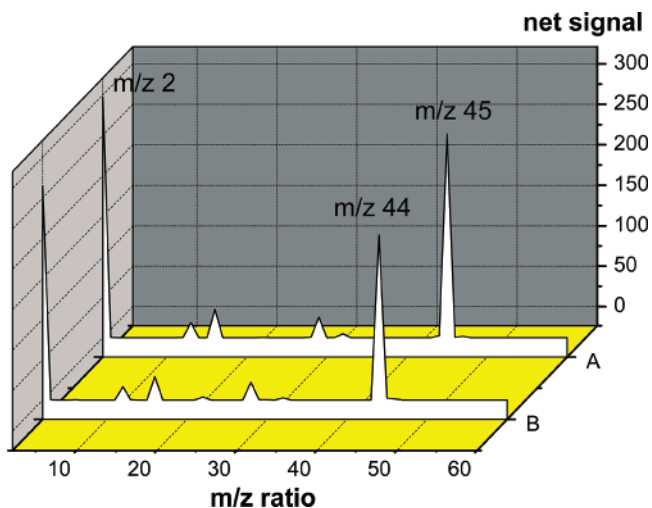
Figure 3. Stacks of gas-phase mass spectra from separate electrolyses of formic acid-^{13}C (trace A) and natural-abundance formic acid (trace B). Actual spectral data points were recorded only at discrete unit m/z values and are displayed here as waterfall traces with the data points connected by interpolate lines.

For reasons of economy, it is highly desirable to reuse the reactor and its supporting equipment for many cycles. Its actual reusability depends on cumulative wear from all reactor operations, such as chemical reactions, repeated pump-downs, positive pressurization from electrogenerated gases, mechanical manipulations, physical transport, and cleanup procedures. To provide some scalar context of reuse, one particular reactor continues to be operational after 25 electrolysis cycles.

To conduct quantitative ^{13}C-isotope determinations, it is paramount that the test system be isolated from surrounding carbonaceous sources, such as air, organic solvents, and organic greases. Toward this end, reliable O-ring compression seals were incorporated into the reactor design to maintain hermetic integrity. As previously mentioned, the reactor was leak-tested by piping it to the gas manifold inlet of a GC-PDHID instrument. Subsequently, its virtual leak rate over 30 min (of static vacuum) was measured to be <1 ppmv carbon dioxide and <15 ppmv air, which is presently acceptable. Turning now to liquid contaminants, one straightforward way to minimize ^{13}C-isotopic dilution by solvents or greases is to exclude their use from the "get-go". Unfortunately, this adopted strategy precludes any addition of most common solvents to the analyte solution (to adjust solubility).

Application of the vacuum electrolysis reactor for isotope testing involves redirection of product focus relative to usual Kolbe processes (here focused more on CO_2). Figure 3 is an *xyy* representation of mass spectra from two electrolyzed formic acids. This type of waterfall graph having discrete data points connected by interpolate lines was chosen to stack multiple spectra in a compact form (actual data were recorded only at unit m/z values). The foreground MS scan (denoted trace B) corresponds to natural formic acid, whereas the background scan is that of formic acid-^{13}C (see trace A). For both cases, the intrinsic ion conductivity of this weak acid was adequate to allow neat electrolysis. Based upon electrogenerated carbon dioxide data, the enriched acid was measured to be 98.9 at. % ^{13}C; utilizing the same reactor under similar conditions, electrolysis of natural formic acid gave 1.2 at. % ^{13}C. The former result was independently tested using 400-MHz

hydrogen FTNMR and found to be 99 at. % ^{13}C. Moreover, the isotopic result obtained for natural formic acid is in favorable agreement with a reference value for natural-abundance carbon (1.1 at. % ^{13}C).[17] Not surprisingly, gas-phase mass spectra from the isotopically distinct formic acids showed product patterns that are consistent with this primary electrolytic reaction:

$$H*CO_2H \rightarrow *CO_2 + H_2$$
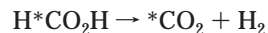
Detected ions of prominence included H_2^+, CO_2^+, CO^+, O_2^+ (from electrolyzed water), O_2^{2+}, and C^+. It should be noted that air leakage into the reactor during analytical operations was crudely monitored by comparison of the baseline MS signal at m/z 40 (argon ion) to the subsequent product MS signal. This turns out to be a practical diagnostic for spotting any major reactor gas leak. Following electrolysis-MS, the formic acid solutions were checked for acidity and found to have pH ~1.

Vacuum electrolysis of acetic acids with four distinct ^{13}C-isotope compositions was investigated. Mass spectra derived from such electrolyses can be viewed in Figure 4 as interpolate waterfall graphs. Figure 4b is an alternate representation of Figure 4a with the m/z scales of the four spectra horizontally aligned. Spectral trace C is that collected from the gas phase of electrolyzed acetic acid-1-^{13}C with ~5 mol % lithium (added to promote solution conductivity). Considering the carbon dioxide results of trace C, isotope enrichment at the C1-position of this acetic acid was calculated to be 99.0 at. % ^{13}C. Under our conditions, the most intense product signals were obtained at m/z 45 and 2, corresponding to $^{13}CO_2^+$ and H_2^+:

$$2CH_3*CO_2H \rightarrow 2*CO_2 + C_2H_6 + H_2$$

In addition, a prominent ion series was detected from m/z 24 to 30. Based upon the reported mechanism for Kolbe electrolysis of acetate,[6,7] it is reasonable to deduce that the source of such ion signals was electrogenerated $^{12}C_2H_6$ (including C_2^+, C_2H^+, $C_2H_2^+$, $C_2H_3^+$, $C_2H_4^+$, $C_2H_5^+$, and $C_2H_6^+$). The net signal measured at m/z 40 (predominantly Ar^+) was small, indeed <0.01% of the base signal at m/z 45. Further, the spectral pattern obtained from m/z 24 to 30 is qualitatively consistent with that of electron-ionized ethane. Thus, it is very likely that the signal detected at m/z 28 was derived from ethane.

Spectral trace D in Figure 4 is that of electrolyzed acetic acid-$^{13}C_2$ with ~10 mol % added lithium. Again, based upon carbon dioxide data, isotope enrichment at the C1-position was measured to be 99.2 at. % ^{13}C. The mass spectrum obtained for acetic acid-$^{13}C_2$ was similar to that of acetic acid-1-^{13}C in the CO_2^+ region. However, the spectral pattern of acetic acid-$^{13}C_2$ was shifted positive by two mass units in the hydrocarbon ion region (here m/z 26−32). Since the synthetic precursors of acetic acid-$^{13}C_2$ were known to have 13-carbon isotope enrichments near 99 at. %, the results again indicate that carbon dioxide was specifically generated from the C1-position.

The observed 2 amu shift in the hydrocarbon region of electrolyzed acetic acid-$^{13}C_2$ positively supports such an interpretation. It should be added that the Ar^+ signal was again small (<0.01%) relative to m/z 45. Not surprisingly, the results above are consistent with the "normal Kolbe process"[9] whereby elec-
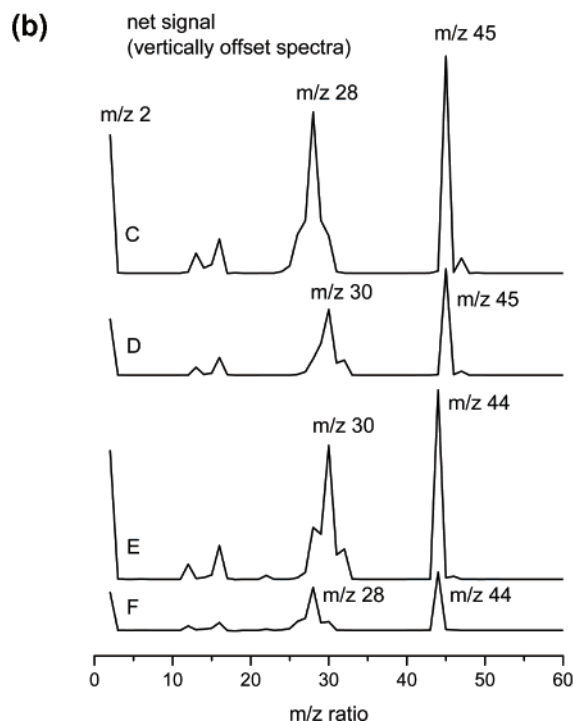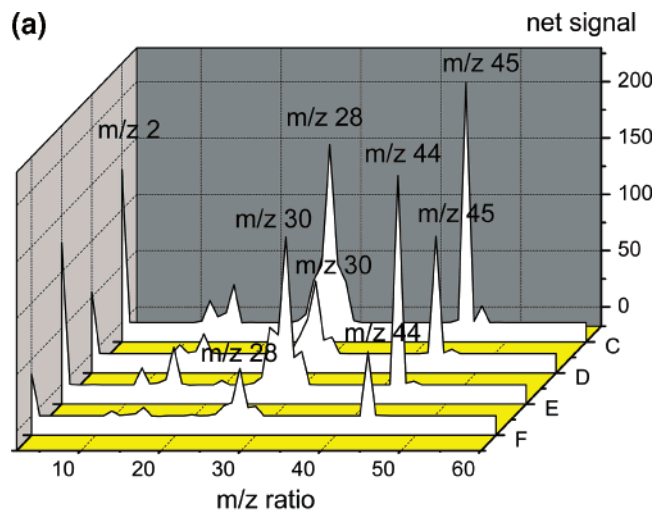
(a) net signal

(b) net signal (vertically offset spectra)

Figure 4. (a) Stacks of gas-phase mass spectra from separate electrolyses of acetic acid-1-^{13}C (trace C), acetic acid-^{13}C$_2$ (trace D), acetic acid-2-^{13}C (trace E), and natural-abundance acetic acid (trace F). Actual spectral data points were recorded only at discrete unit m/z values and are displayed here as waterfall traces with the data points connected by interpolate lines. (b) Alternate representation of (a) depicting four mass spectra from acetic acid electrolyses (traces C–F). Here, the m/z scales are aligned for each spectrum.

trolysis of acetic acid-^{13}C$_2$ would generate ^{13}C$_2$H$_6$ as its major electroorganic product.

Trace E in Figure 4 is a gas-phase spectrum of electrolyzed acetic acid-2-^{13}C with ~5 mol % added lithium. For this case, isotopic analysis of the precursors indicated that the C1-position should be depleted in 13-carbon (relative to natural abundance) whereas the C2-position should be highly enriched (~99 at. % ^{13}C). Indeed isotopic measurement of the carbon dioxide region for electrolyzed acetic acid-2-^{13}C gave 0.8 at. % ^{13}C, with strong signals obtained at m/z 44 and 2. In addition, the hydrocarbon ion series was observed from m/z 26 to 32. By comparison to acetic acid-

Table 1. ^{13}C-Isotopic Enrichment Results Using the Vacuum Electrolysis Reactor

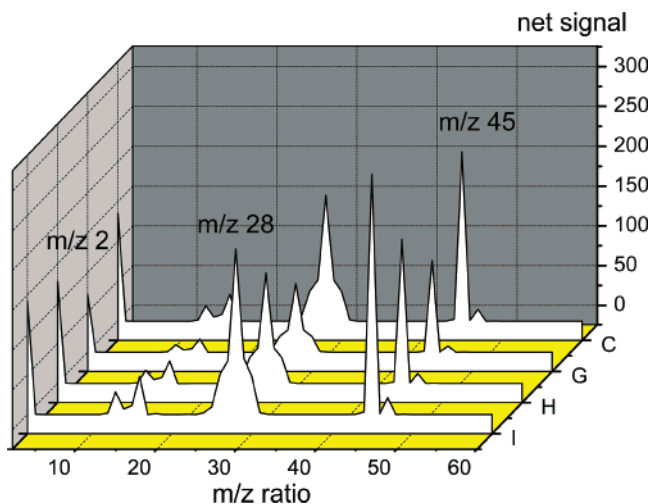|	at. % ^{13}C	
	actual	expected
formic acid natural	1.2	1.1
formic acid-^{13}C	98.9	99
acetic acid natural	1.2	1.1
acetic acid-1-^{13}C	99.0	99
acetic acid-2-^{13}C	0.8	<1.1
acetic acid-^{13}C$_2$	99.2	99

net signal

Figure 5. Stacks of gas-phase mass spectra from separate electrolyses of the same batch of acetic acid-1-^{13}C (traces C and G–I). The intertrace variability in net signal values is mainly due to different gas pressures in the mass spectrometer for each trace. Actual spectral data points were recorded only at discrete unit m/z values and are displayed here as waterfall traces with the data points connected by interpolate lines.

^{13}C$_2$ results, it follows that electrolysis of acetic acid-2-^{13}C should generate ^{13}C$_2$H$_6$ as its main organic product. Finally, trace F in Figure 4 is a spectrum of electrolyzed natural acetic acid. Here the highest signals were also measured at m/z 44 and 2; moreover, the familiar hydrocarbon series was observed from m/z 24 to 30. Analysis of natural acetic acid resulted in an enrichment value of 1.2 at. % ^{13}C. In summary the results from Figures 3 and 4 are self-consistent with the principle of selective carbon dioxide generation from the acetate C1-position (see Table 1).

To characterize the precision of this reactor technique, replicate electrolyses were implemented on one batch of acetic acid. Figure 5 contains four gas-phase spectra (traces C and G–I, displayed as waterfall graphs) from electrolyzed acetic acid-1-^{13}C with ~5 mol % added lithium. For each electrolytic trial, the mass pattern matched that described above for acetic acid-1-^{13}C (including ^{13}CO$_2^+$, H$_2^+$, ^{12}C$_2$H$_X^+$, O$_2^{2+}$, and C$^+$). Measurement of 13-carbon enrichment based upon the carbon dioxide region gave the following: 99.0, 99.0, 98.9, and 98.9 at. %. Accordingly, the standard deviation of the present isotope measurement system is estimated to be ±0.1 at. % ^{13}C.

Variant chemical procedures were developed to effect electrolysis of different carboxylic acids. For the simplest case, formic acid was degassed and electrolyzed neat. However, to achieve
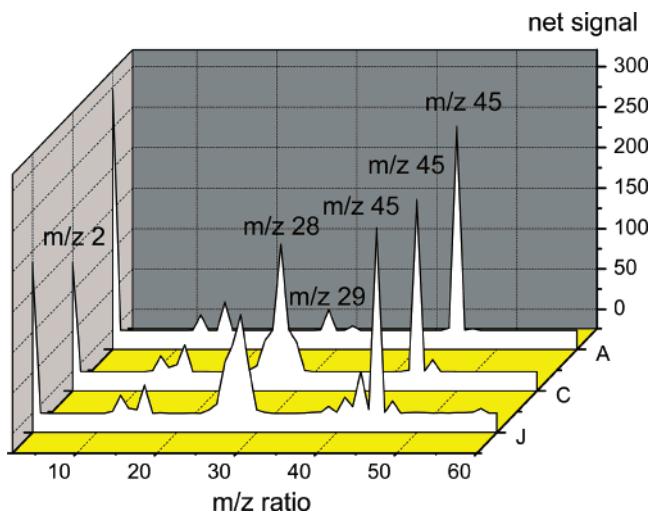
Figure 6. Stacks of gas-phase mass spectra from separate electrolyses of formic acid-^{13}C (trace A), acetic acid-1-^{13}C (trace C), and propionic acid-1-^{13}C (trace J). The pre-electrolysis chemical treatment of each carboxylic acid varied (see main text for detail). Actual spectral data points were recorded only at discrete unit m/z values and are displayed here as waterfall traces with the data points connected by interpolate lines.

adequate solution conductance, it proved necessary to add ~5 mol % lithium to acetic acid. For yet higher carboxylates, a three-component mix was developed consisting of acid, lithium hydroxide, and water. Indeed, it was possible to both solubilize and electrolyze propionic acid using such mix. Figure 6 shows gas product spectra for three electrolyzed carboxylic acids: formic acid-^{13}C in trace A, acetic acid-1-^{13}C in trace C, and propionic acid-1-^{13}C in trace J. The mass spectrum of propionic acid-1-^{13}C was more complex relative to the others, with strong signals observed at m/z 45, 2, and 28. Also detected was an ion series from m/z 36 to 59, including notable signals at m/z 39, 41, 43, 45, 47, and 58. Now this latter signal can be assigned to $^{12}C_4H_{10}^+$, whereas the remaining ions are likely derived from carbon dioxide and butane. The pattern obtained in the C_3H_x hydrocarbon region is consistent with butane fragments, since a minor signal was present at m/z 36 as well as stronger ones at m/z 39, 41, and 43. Unfortunately, the measured isotope enrichment for propionic acid-1-^{13}C was found to be only 98.0 at. % ^{13}C. The latter result is ~1-at. % lower than the expected ^{13}C1 value based upon precursor ^{13}C-isotope information, and it suggests overlapping mass signals from butane fragments and carbon dioxide.

During vacuum electrolysis of carboxylic acids, the instantaneous current varied while a fixed voltage was supplied (range 10−25 V). The constant supply voltage was empirically chosen such that an adequate amount of carbon dioxide was generated for mass spectrometry. To provide some context, at 25 V applied the current ranged from 0.011 to 0.015 A for formic acid. Thus, the electric charge passed over 30 min is calculated to be 25 C for formic acid (likewise 40 C for acetic acid experiments). Given an assumption that the only electrogenerated gases were CO_2,

H_2, and C_2H_6, then the maximum reactor pressures can be estimated as 0.3 atm for formic acid and 1.0 atm for acetic acid.

A detailed calculation using CO_2^+ mass spectra to estimate ^{13}C-enrichment should include the data from m/z 44 to 49. For example, one can define an appropriate sum of squares error (SSE) parameter and conduct some least-squares search.[15] Given the variable assignment [x] = at. % ^{12}C, then [1 − x] = at. % ^{13}C; similarly, [y] = at. % ^{16}O, [z] = at. % ^{17}O, and [1 − y − z]= at. % ^{18}O. Next the spectral signals from m/z 44 to 49 can be normalized (denoted Nmz) such that their summation is unity. Each algebraic mass term is then (nonequally) weighted to give a useful SSE parameter for CO_2 isotope enrichment:

$$
\begin{aligned}
SSE = \ &w1[Nmz44 - xyy]^2 + \\
&w2[Nmz45 - 2xyz - (1 - x)^*yy]^2 + \\
&w3[Nmz46 - 2xy(1 - y - z) - xzz - 2(1 - x)yz]^2 + \\
&w4[Nmz47 - 2xz(1 - y - z) - 2(1 - x)y(1 - y - z) - (1 - x)zz]^2 + \\
&w5[Nmz48 - 2(1 - x)z(1 - y - z) - x(1 - y - z)(1 - y - z)]^2 + \\
&w6[Nmz49 - (1 - x)(1 - y - z)(1 - y - z)]^2 \quad\quad (1)
\end{aligned}
$$

The w(i) values above represent weight factors that are proportional to the associated signal magnitude within each term. By applying eq 1 to the electrolysis results, reasonable 12-carbon, 13-carbon, 16-oxygen, 17-oxygen, and 18-oxygen atom percent values were realized.

The present methodology can involve addition of reactants such as lithium, lithium hydroxide, and purified water to the acid. It is important that any additives do not introduce significant amounts of 12-carbon to the analyte solution. One notable feature here is the electrolysis of acidic pH solutions. This was deliberately intended to minimize any accumulation of natural-abundance bicarbonate in pre-electrolysis mixes, which could later interfere with ^{13}C-isotope determinations. From this work, it is notable that the electrogenerated $^{13}CO_2$ was quantitatively obtained from the C1-position of formate or acetate.

Overall, the present electrolysis results are rather consistent with reaction schemes reported for the Kolbe process. Electrolysis of small carboxylic acids here generated carbon dioxide and hydrogen, along with observable amounts of carbon monoxide (formate), or ethane (acetate), or butane (propionate). The authors propose that the vacuum electrolysis reactor represents an incremental innovation compared to antecedent gastight electrochemical cells,[18,19] since this small gizmo permits vacuum operations, select reactions, forced stirring, and electrolysis all at the analytical scale. Indeed, the scope of technical applications for this robust reactor seems broad since it can be readily interfaced to gas analyzers.

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