analytical chemistry

Technical Note

A dual-stage consumable-free thermal modulator for the hyphenation of thermal analysis, gas chromatography and mass spectrometry (TA-GC-MS)

Sebastian Wohlfahrt, Michael Fischer, Janos Varga, Mohammad Reza Saraji-Bozorgzad, Georg Matuschek, Thomas Denner, and Ralf Zimmermann

Just Accepted

ACS Publications

A dual-stage consumable-free thermal modulator for the hyphenation of thermal analysis, gas chromatography and mass spectrometry (TA-GC-MS)

Sebastian Wohlfahrt[†‡], Michael Fischer[†‡], Janos Varga[‡⊥], Mohammad-Reza Saraji-Bozorgzad[§], Georg Matuschek[†], Thomas Denner[♯], Ralf Zimmermann[†‡*]

[†] Joint Mass Spectrometry Centre, Helmholtz Zentrum Muenchen, Comprehensive Molecular Analytics, 85764 Neuherberg, Germany

[‡] Joint Mass Spectrometry Centre, University Rostock, Chair for Analytical Chemistry, 18059 Rostock, Germany

[⊥] University of Augsburg, Chair of Resource Strategy, 86159 Augsburg, Germany

[§] Photonion GmbH, 19061 Schwerin, Germany

[♯] Netzsch-Geraetebau GmbH, 95100 Selb, Germany

ABSTRACT: The design of the so-called "Peltier modulator" is presented. It is a new dual-stage consumable-free thermal modulator for TA-GC-MS. It requires only electrical power for operation as it facilitates thermo-electric coolers instead of cryogenics for trapping and resistive on-column heating for re-injection. Trapping and desorption temperatures, as well as modulation cycles are freely adjustable. The stationary phase for the trapping region can be selected to suit the specific application, since common fused silica capillary is used. The Peltier modulator's performance is demonstrated with a broad range of different standard substances and with heavy crude oil as a complex real life sample. Successful modulation from n-pentane to pyrene (boiling points = 36/394 °C) is presented. The produced peaks show the narrowest bandwidths ever reported for a consumable-free thermal modulator, i.e. 12.8±1.2 ms for n-pentadecane. The Peltier modulator is rugged, cost effective, requires low maintenance and decreases security issues significantly, compared to commercial available solutions using liquid N_2/CO_2.

Thermal Analysis (TA) gives information about heat-dependent physical properties of a sample. During the heating process, the sample undergoes evaporation and/or decomposition which lead to evolving gases. These gases can be characterized by mass spectrometry (MS)[1] to gain insight into their chemical composition.

The combination of TA and MS was introduced in the 1970s and improved continuously. In most cases, electron ionization (EI) at 70 eV is applied. A "softer", that means lower energetic alternative for EI, is the application of single photon ionization (SPI) with photon energies around 10 eV. Geissler et al. used the reduced fragmentation with SPI to distinguish between different crude oils with TA-SPI-MS.[2] Recently, Photonion GmbH (Schwerin, Germany) presented the first commercial available TA-SPI-MS system together with Netzsch-Geraetebau GmbH (Selb, Germany).

One step further is the combination of TA-MS with an additional gas chromatographic (GC) step to form TA-GC-MS. These systems are applied to analyze complex gas mixtures, for example during lignite pyrolysis[3] or to quantify functional groups[4]. In these two cases, only a split of the effluent, which is of special interest, is transferred from the TA and then undergoes a complete GC-MS run (heart-cutting).

Another approach is the quasi-continuous transfer of the TA effluent by trapping and re-injection into the GC (comprehensive) through a modulator. The gas chromatographic step is a fast one with a short separation column (≤ 3 m). The character of this approach is, to a certain extent, similar to comprehensive two-dimensional GC-MS (GC×GC-MS), but with TA as first dimension. A similar system that facilitates a cryogenic liquid CO_2 modulator was used by the authors for example to follow the decomposition of plastics or to characterize petrochemical samples such as diesel or even crude oil.[5,6]

Although the overall performance of the applied liquid CO_2 modulator was sufficient, some drawbacks, such as high cryogen consumption or the influence of the GC on the trapping temperature, lead to the plan to design a modulator especially for TA-GC-MS. The key requirements were as follows: the modulator should be consumable-free (run only on electrical power), rugged, flexible in regards to temperature and time settings and should compete with the performance of a CO_2 modulator. There are three main groups of modulators on the market today:

1. Valve-based modulators: A sample loop is filled with effluent from the first dimension. After a certain time a valve, usually a high-temperature valve inside the GC oven, switches and the sample is transported into the second dimension through an auxiliary gas flow.[7,8] It is well suited and often applied for heart-cutting TA-GC-MS.[9] But the applicability of the valves is usually limited to a specific working temperature range and sample volume and the analytes are not accumulat-

ed/re-focused. The latter is an important factor, especially in trace analysis.

2. Differential flow modulation also facilitates a sample loop and primary and auxiliary flows. Seeley et al. were the first to report on this kind of modulator in 2000.[10] Since then it emerged to one of the most abundant modulator techniques in GC×GC. Because flow modulation requires high flow rates in the second dimension (about 20 times higher than in the 1. dim.) it is mainly used in combination with flame ionization detectors (FID).[11] Flow-splitting prior to detection[12] is one ambition to enhance the suitability in combination with MS. Unfortunately, the lack of active flow from the TA (the high vacuum in the MS is the only driving force for analyte transport) limits the applicability of flow modulation in TA-GC-MS.

3. Thermal modulators were the first ones reported in the beginning of GC×GC.[13] They can be divided into those using cryogenics (i.e. CO_2/N_2) and those without consumables (consumable-free).

Modulators working with liquid CO_2/N_2 represent the majority in GC×GC-MS nowadays.[14] They reach very low temperatures in short time. Desorption of the trapped analytes is either done via with free thermal convection, a counter hot jet or on-column resistive heating. These systems deliver probably the best performance on the market. One major disadvantage is their high demand for cryogenics, which is a safety and also a reasonable cost issue.

Therefore, thermal modulators without cryogenics have been developed in the last years. Zoex for example, offers an alternative for their liquid N_2-cooled system: a closed cryo-cooler circuit cools a jet down to -90 °C (ZX2, Zoex Corp., Houston, USA), but gaseous nitrogen is still needed for the cold/hot jet.

Another approach, also using some kind of cold jet, was presented by Panic et al. in 2011.[15] They used compressed air and a vertex cooler to cool a metal capillary outside a common GC oven to a minimum of -20 °C. They were able to trap substances down to a level of n-hexane. Resistive heating was done through direct capacitor discharge on the capillary. The system is very user-friendly, robust and performs well, but our aim was to achieve lower trapping temperatures.

A solution without a cold jet was presented by Libardoni et al.: they realized a modulator with on-column resistive heating of a metal capillary, which was placed inside a closed cryo-cooled refrigerant circuit at about -33 °C.[16] Even trapping of pentane was possible with this setup but the modulators performance was dependent on the GC temperature as it is placed inside.

Kim et al. chose another way of cooling. They employed a thermo-electric cooler, a Peltier element, for cooling and resistive heating for desorption purposes in their miniaturized GC×GC system.[17] Muscalu et al. also used thermo-electric coolers to operate a single-stage consumable-free modulator for GC×GC-μECD.[18]

Extracting the advantages of the aforementioned concepts and keeping the special requirements of TA-GC-MS in mind, we developed a modulator that uses multi-stage Peltier elements for trapping and resistive heating of common stainless steel capillary for desorption, the so-called Peltier modulator. It is a consumable-free thermal modulator that is rugged, highly flexible regarding desorption temperature and modulation cycle. It provides high thermal performance and uses only electrical power.

In this study, the performance of the Peltier modulator is evaluated concerning its thermal behavior (trapping capabilities, injection band widths) and compared to other modulator concepts. Its applicability for TA-GC-MS is demonstrated with standard substances as well as with measurements of heavy crude oil as a complex real life sample.

EXPERIMENTAL

System and mounting

In this study, the modulator was integrated into a hyphenated thermal analysis-mass spectrometry (TA-MS) system consisting of a thermobalance (Jupiter F3, Netzsch, Selb, Germany) and a time-of-flight MS (HTOF, Tofwerk, Thun, Switzerland). Electron ionization at 70 eV was used for the injection bandwidth characterization and single photon ionization (SPI) with a custom made light source (PKS 106 PID lamp, Heraeus Noblelight, Hanau, Germany) at 10.6 eV was applied for the crude oil measurements.

A heated transfer line (250/300 °C) leads the evolving gases from the TA to a temperature adjustable home-built interstage oven. The oven sits on top of the mass spectrometer's ionizer inlet and houses the connections to and from the modulator. The Peltier modulator is then connected to a 3 m RTX50 column (0.25 mm ID, 0.25 μm, Restek, Bellefonte, USA) to give a TA-GC-MS system. A scheme of this setup is shown in **Figure 1a**. For a more detailed view, see **Figure S-1** within the Supporting Information.

The Peltier modulator is mounted outside, thus its performance is not affected by the temperature inside the oven and vice versa, the GC oven temperature is not affected by the modulator. The Peltier modulator's trapping and desorption temperature remains the same. To compare this fact, we conducted measurements with a liquid CO_2 modulator inside a commercial GC×GC system (Thermo Trace GC×GC, ThermoFisher Scientific, Waltham, USA). Within a 25–250 °C GC ramp the trapping temperature rose from -67 °C to 95 °C ($\Delta T = 167$ °C) . While this might be no problem in GC×GC, since the volatility of the analytes is usually decreased with proceeding GC ramp, it might cause problems in TA-GC-MS. Especially in pyrolysis of complex organic samples, small and highly volatile as well as larger and lower volatile molecules evolve simultaneously. A decreased performance of the modulator could lead to analyte breakthrough.

Apparatus

A schematic of the developed Peltier modulator is depicted in **Figure 1b**. It consists of two main parts: two opposing three-stage Peltier elements (1) and two so-called inlays in sandwich configuration between them.

The Peltier elements are common thermoelectric coolers (TEC3-127-71-31-06, Conrad Electronics, Hirschau, Germany) with a maximum temperature difference (ΔT; given by manufacturer) between the hot/cold side (A)/(B) of 97 °C. They are constantly operated at 8 A/14 V DC.

The inlays consist of common stainless steel capillary (2) with an inner diameter (ID) of 0.53 mm (IP Deactivated MXT, Restek, Bellefonte, USA) with electrical connections (3) made from 3 mm welding wire. Through the metal capillary, normal fused silica column is fed (4). The only limiting parameter for the choice of analytical column is the ID of the metal capil-

lary. In this study, about 0.5 m mid-polar RTX50 column (0.25 mm ID, 0.25 μm, Restek, Bellefonte, USA) was used. The contact area between inlays and cold sides was increased by some layers of Kapton® film (5) to ensure sufficient heat flow and increase cooling performance.

To reach minimal temperatures at the Peltier's cold side, the hot side has to be cooled. We found active water cooling with a chipset cooler (twinplex, AquaComputer, Gleichen, Germany) in a closed circuit to a low-temperature thermostat employing water at about 2 °C as coolant to fit best. Minimum temperatures of about -60 °C were achieved inside the inlays during operation.

The modulator is controlled through different units. A detailed description, including a scheme of these units and the mode of operation, can be found in the Supporting Information (Controlling units and operation).
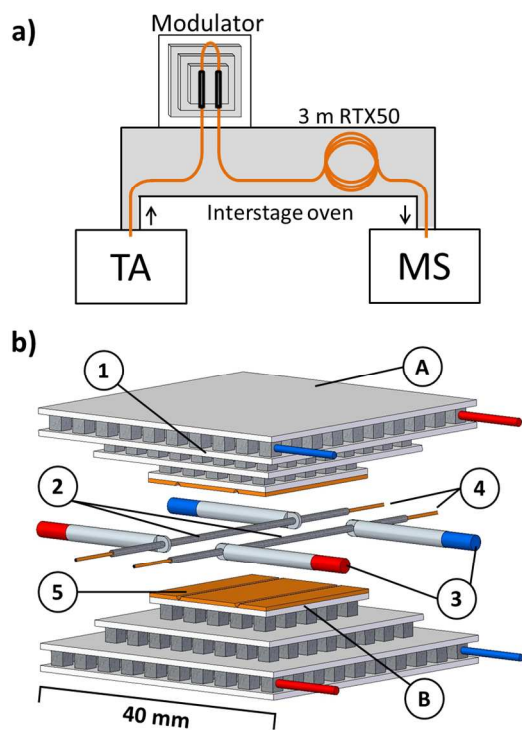

Figure 1. a) The Peltier modulator was integrated into a TA-MS system. Together with a short GC separation, this results in a TA-GC-MS system. **b)** Major setup of the Peltier modulator: (1) two opposing three-stage Peltier elements with a hot/cold side A/B; (2) two inlays made from stainless steel capillary with welding wire as electrical connections (3); (4) fused silica column; (5) some layers of Kapton® film to increase the heat flow.

RESULTS AND DISCUSSION

Modulator cooling and heating

Minimum inlay temperatures of -60 °C were reached during operation. Substances $\geq C_5$ (n-pentane) were trappable at these conditions on a mid-polar Restek RTX50 with a 0.25 μm phase. Please note that the lower limit, to where substances are trappable, depends highly on the trapping capillary's stationary phase. In case of a thicker and lower polarity phase, even butane or propane might be trappable at -60 °C. For example, Panic et al. were able to trap pentane (as a component in gasoline) with a 1 μm polydimethylsiloxane phase at -20 °C.[15]

During the heating pulses, cooling is overcompensated and the inlay reaches the desired, freely adjustable desorption temperature. In this study it was set to about 310 °C.

Detailed information on the heating and cooling behavior is given in the Supporting Information (Modulator heating and cooling).

Modulation cycles

A typical complete modulation cycle for the applied TA-GC-MS system takes 30 s with 3 s-heating pulses. Nevertheless, cycle times can be chosen freely. An upper limit is not defined. Successful measurements with a minimum modulation cycle of 4 s with n-hexane were conducted (see **Figure S-4**). For modulation cycles shorter than 30 s the default desorption time of 3 s was shortened accordingly.

Modulator performance - injection bandwidths

One major performance benchmark for modulators is the injection bandwidth. It should be as narrow as possible to ensure high peak capacity. The reported peak widths with resistively heated modulators were relatively poor in comparison to cryogenic modulators until the publications of Libardoni and Panic.[15,16] They presented peaks widths (FWHM) as low as 20 and 60 ms, respectively. The Peltier modulator in turn also delivers high-end performance and, to the best of the author's knowledge, produces the narrowest peaks ever reported with a consumable-free modulator.

To demonstrate this, a selection of n-alkanes and aromatics/polyaromatic hydrocarbons with a broad boiling point (bp) range were consecutively introduced as head space samples in nitrogen carrier gas from the thermobalance to the modulator and measured by EI-TOF-MS in modulation cycles of 30 s. In this case about 1 m of uncoated transfer line was used to connect the Peltier modulator and the MS, which gives an average velocity and outlet flow of 1.4 m/s and 1.57 ml/min, respectively (calculated with Agilent's "Pressure Flow Calculator"). The acquisition rate was set to 200 Hz. The overall settings, despite the TA temperature, remained constant for all tested substances. Peak widths were calculated by interpolating between data points of the total ion count (TIC). The results are shown in **Figure 2** as mean values with standard deviation (N=5; C_5–C_{20}: black rectangles; B benzene, X p-xylene, N naphthalene, F fluorene, A anthracene, P pyrene: red dots). The detailed values can also be found in **Table S-1**.

The calculated injection bandwidths were as narrow as 12.8±1.2 ms (C_{15}, pentadecane). Widths below 25 ms were accessible for a wide range of substances (C_6–C_{20}, bp = 69–343 °C). Below and above these boiling points, peak widths increased moderately, i.e. to 44.4±7.6 ms for pentane (C_5, bp = 36 °C) and 43.9±2.9 ms for pyrene (P, bp = 394 °C). These values are still in the same range or even lower than those produced with cryogenic modulation.[19]

An explanation for the observed peak broadening with highly volatile analytes cannot be given at the moment. The same effect was reported by Libardoni et al.[16] Overall, peak widths of volatile substances are highly dependent on the analyte concentration. Overloading of the modulator can result in broad peaks (up to 500 ms) and or odd peak shapes (e.g. peak splitting).
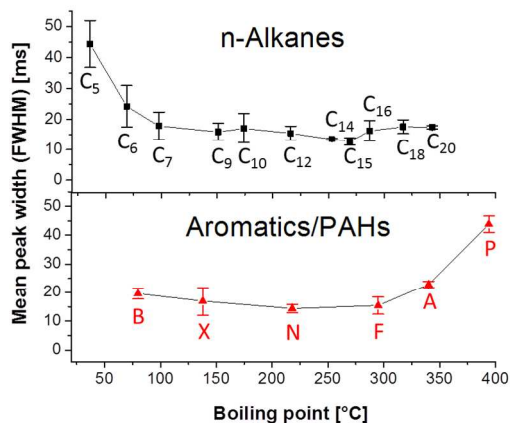
Figure 2. Peak widths at half maximum versus boiling point of a selection of n-alkanes (C_5–C_{20}: black rectangles) and aromatics/polyaromatic hydrocarbons (B benzene, X p-xylene, N naphthalene, F fluorene, A anthracene, P pyrene: red triangles). Results were obtained by TA-Modulator-MS with electron ionization at 200 Hz acquisition rate. The TIC was taken for calculation.

Applications

Additionally to the measurements conducted with standard substances, crude oil as a real world, complex organic sample was analyzed by TA-Modulator-MS and TA-GC-MS, respectively. A very heavy Turkish crude oil, which was already characterized in previous studies and is known to have a distinct distillation and pyrolysis phase, was used.[2,6]

First, the same setup as for the injection bandwidth measurements was used (direct connection of the modulator to the MS, modulation cycle = 30 s), but with SPI instead of EI and the interstage oven at 300 instead of 250 °C. The sample was heated with 10 K/min from 50−550 °C.

The TIC (black) and the mass loss signal (blue) in dependence to the TA temperature are shown in **Figure 3a**. The TIC displays unobstructed analyte pulses that are released from the modulator, even at higher temperatures. For verification, three mass traces (m/z 96, 176 and 260; red) are extracted from the TIC and displayed separately in **3b**. For a better view, signals of m/z 176 from two modulation cycles are zoomed in **3c**. No peak broadening is visible, even with substances that evolve during the pyrolysis of this heavy crude oil at temperatures of about 450 °C.

Second, the same sample was analyzed with an additional short GC column to gain separation of the analytes (**Figure 4**). To increase the separation space, the interstage oven temperature was ramped from 110−300 °C with 8 K/min (blue line, **4a**). The mass loss signal is identical to the one without GC and therefore not shown. The extracted SIC of m/z 176 looks familiar to the one in **3b**, at first sight. A detailed visualization is shown in **Figure 4c** with a two dimensional contour plot. Here, the retention time of m/z 176 is shown in dependence to the TA temperature. Two distinct traces are visible in the region of 150−310 °C (evaporation phase) and from 375−520 °C (pyrolysis phase).

In former publications, the benefit or a higher resolving power (R = M/ΔM) of the applied MS was mentioned in order to differentiate between isobaric compounds.[6] In this study, the MS is capable of that (R_{max} = 4000). The two signals reveal two different exact masses (**4d**): (1) m/z 176.15 and (2) m/z

176.07. A specific identification is not possible at this resolution and mass accuracy of 20 ppm, but with the knowledge of common substance classes present in heavy crude oils, it is likely that (1) represents isomers of monoaromatics with the sum formula $C_{13}H_{20}$ and (2) might be a signal of heterocyclic benzothiophene isomers with the sum formula $C_{11}H_{12}S$.[20]

Even if the resolving power is not comparable to a high-resolution TOF-MS (R_{max} = 10000−50000; e.g. Leco HRTOF), the exact mass signals enable the differentiation between isobaric substances directly and not only according to the retention time behavior, as before.[5,6]
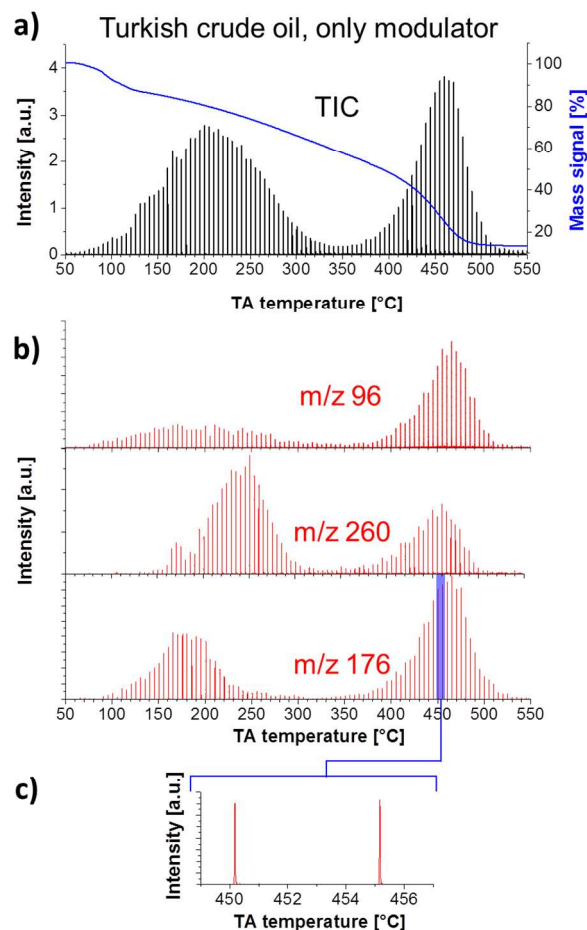

Figure 3. a) Total ion count **(**TIC, black lines) from TA-GC-MS with SPI and the respective mass signal (blue line) of a Turkish crude oil in dependence to TA temperature. The TIC displays unobstructed analyte pulses. **b)** Mass traces of m/z 96, 176 and 260 (red lines. **c)** Two modulation cycles of m/z 176 are zoomed. No peak broadening is visible.

CONCLUSIONS

The design and first evaluation of a newly developed consumable-free dual-stage thermal modulator has been described. Its performance was compared to data reported for cryogenic and consumable-free modulators. Successful modulation of a wide range of substances up to pyrene (bp = 394 °C) without any setting changes has been presented. To the best of the author's knowledge, the produced peaks show the narrowest bandwidths (FWHM) ever reported for a consumable-free thermal modulator so far.

The Peltier modulator proved to be rugged and stable since no performance loss or breakage occurred in several thousands of modulation cycles. It is highly flexible concerning modulation cycle and desorption time. Trapping and desorption temperatures are adjustable and the stationary phase for the trapping region can be chosen to suit the specific application.
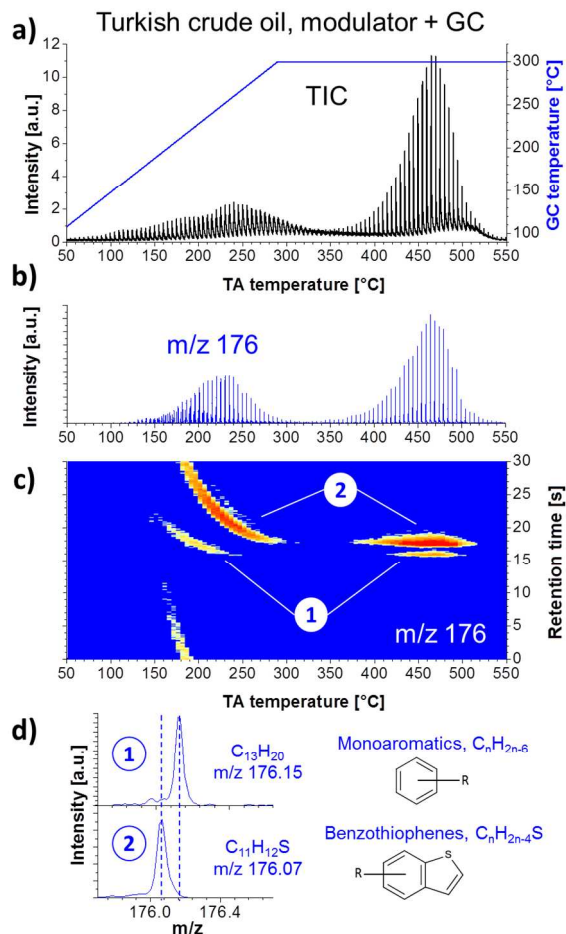

Figure 4. a) TIC (black lines) and GC (interstage oven) temperature (blue line) in dependence to TA temperature of a TA-GC-MS measurement of the same Turkish crude oil as in Fig 3. **b)** Mass trace of m/z 176. **c)** Contour plot of m/z 176: retention time against TA temperature. **d)** The exact masses of the signals are different: 176.15 (1) and 176.07 (2) and can be assigned to the substances with the sum formula $C_{13}H_{20}$ and $C_{11}H_{12}S$, respectively.

The Peltier modulator is cost effective, requires low maintenance, e.g. no change of gas cylinders, and lowers security issues significantly compared to commercial available solutions using liquid N_2/CO_2.

The overall design is well suited for implementation into existing system offering an online gas source. In this study, a hyphenation of thermal analysis, gas chromatography and mass spectrometry was used. The combination with a new fast-GC, reported recently by Fischer et al.[21], will be subject of an upcoming study.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS publications website at DOI: xx.
Figure S-1–4: Additional information on the overall setup, details on the construction of the Peltier modulator and the controlling units
Figure S-5–6, Table S-1: Data on heating/cooling performance and injection bandwidths

AUTHOR INFORMATION

Corresponding Author

* E-mail: ralf.zimmermann@helmholtz-muenchen.de. Tel.: +49 (0) 89 3187 4544.

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

REFERENCES

(1) Materazzi, S.; Risoluti, R. *Appl. Spectrosc. Rev.* **2014**, *49*, 635-665.
(2) Geissler, R.; Saraji-Bozorgzad, M.; Streibel, T.; Kaisersberger, E.; Denner, T.; Zimmermann, R. *J. Therm. Anal. Calorim.* **2009**, *96*, 813-820.
(3) He, Q.; Wan, K.; Hoadley, A.; Yeasmin, H.; Miao, Z. *Fuel* **2015**, *156*, 121-128.
(4) Hof, F.; Schäfer, R. A.; Weiss, C.; Hauke, F.; Hirsch, A. *Chemistry – A European Journal* **2014**, *20*, 16644-16651.
(5) Saraji-Bozorgzad, M. R.; Eschner, M.; Groeger, T. M.; Streibel, T.; Geissler, R.; Kaisersbeiger, E.; Denner, T.; Zimmermann, R. *Anal. Chem.* **2010**, *82*, 9644-9653.
(6) Wohlfahrt, S.; Fischer, M.; Saraji-Bozorgzad, M.; Matuschek, G.; Streibel, T.; Post, E.; Denner, T.; Zimmermann, R. *Anal Bioanal Chem* **2013**, *405*, 7107-7116.
(7) Wang, F. C. Y. *J. Chromatogr. A* **2008**, *1188*, 274-280.
(8) Siegler, W. C.; Fitz, B. D.; Hoggard, J. C.; Synovec, R. E. *Anal. Chem.* **2011**, *83*, 5190-5196.
(9) Conterosito, E.; Palin, L.; Antonioli, D.; Viterbo, D.; Mugnaioli , E.; Kolb, U.; Perioli, L.; Milanesio, M.; Gianotti, V. *Chemistry – A European Journal* **2015**, n/a-n/a.

(10) Seeley, J. V.; Kramp, F.; Hicks, C. J. *Anal. Chem.* **2000**, *72*, 4346-4352.

(11) Duhamel, C.; Cardinael, P.; Peulon-Agasse, V.; Firor, R.; Pascaud, L.; Semard-Jousset, G.; Giusti, P.; Livadaris, V. *J. Chromatogr. A* **2015**.

(12) Costa, R.; Fanali, C.; Pennazza, G.; Tedone, L.; Dugo, L.; Santonico, M.; Sciarrone, D.; Cacciola, F.; Cucchiarini, L.; Dachà, M.; Mondello, L. *LWT - Food Science and Technology* **2015**, *60*, 905-913.

(13) Liu, Z.; Phillips, J. B. *J. Chromatogr. Sci.* **1991**, *29*, 227-231.

(14) Stefanuto, P.-H.; Perrault, K.; Stadler, S.; Pesesse, R.; LeBlanc, H.; Forbes, S.; Focant, J.-F. *Anal. Bioanal. Chem* **2015**, *407*, 4767-4778.

(15) Panic, O.; Gorecki, T.; McNeish, C.; Goldstein, A. H.; Williams, B. J.; Worton, D. R.; Hering, S. V.; Kreisberg, N. M. *J. Chromatogr. A* **2011**, *1218*, 3070-3079.

(16) Libardoni, M.; Fix, C.; Waite, J. H.; Sacks, R. *Anal. Meth.* **2010**, *2*, 936-943.

(17) Kim, S. J.; Serrano, G.; Wise, K. D.; Kurabayashi, K.; Zellers, E. T. *Anal. Chem.* **2011**, *83*, 5556-5562.

(18) Muscalu, A. M.; Edwards, M.; Górecki, T.; Reiner, E. J. *J. Chromatogr. A* **2015**, *1391*, 93-101.

(19) Tranchida, P. Q.; Zoccali, M.; Franchina, F. A.; Dugo, P.; Mondello, L. *J. Sep. Sci.* **2013**, *36*, 212-218.

(20) Altgelt, K. H.; Boduszynski, M. M. *Composition and Analysis of Heavy Petroleum Fractions*; Marcel Dekker, Inc.: New York, 1994.

(21) Fischer, M.; Wohlfahrt, S.; Varga, J.; Matuschek, G.; Saraji-Bozorgzad, M. R.; Denner, T.; Walte, A.; Zimmermann, R. *Anal. Chem.* **2015**, *87*, 8634-8639.

for TOC only