

Supplementary Material

Comparison of conventional and microwave heating for evaluation of microwave effects

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Equipment for oil bath heating experiments

Conventional heating experiments (Fig. S1 (a)) were performed using a standard IKA hot plate – magnetic stirrer (IKA Works GmbH & Co. KG, Germany), with 300 ml pre-heated silicone oil bath. Stirring speed was set to 700 rpm. Oil bath temperature was controlled and constantly monitored by precise IKA ETS-D5 contact thermometer.

Standard 10 ml volume cylindrical Pyrex[®] reaction vessels (inner diameter 12 mm; obtained from CEM Corporation, USA) were used, equipped with identical, small cylindrical stir bars. The vessels were sealed by a closing cover assembly connected to an external pressure sensor. Internal fiber optic probe protected by glass thermowell with high thermal conductivity sapphire tip (CEM Corporation, USA) was used to monitor temperature. The fiber optic sensor's signal was recorded through the CEM Discover[®] microwave instrument, in order to exclude any errors from the different read-out instrumentation.

Equipment for microwave heating experiments

Microwave irradiation experiments (Fig. S1 (b)) were performed using single-mode CEM Discover[®] Systems (CEM Corporation, USA). Experiments were performed either in temperature control mode or in constant power mode. Stirring speed was set to “High” (ca. 700 rpm).

Standard 10 ml volume cylindrical Pyrex[®] reaction vessels (inner diameter 12 mm; obtained from CEM Corporation, USA) were used, equipped with small cylindrical stir bars. The vessels were sealed by a closing cover assembly connected to an external pressure sensor. Internal fiber optic probe (identical to oil bath heating experiments) protected by glass thermowell with high thermal conductivity sapphire tip (CEM Corporation, USA) was used to monitor temperature.

In the FO controlled MW experiments (besides the FO temperature) the signal of the IR temperature sensor in the same microwave reactor was also monitored simultaneously, using the data that can be extracted from the IP packets sent on the LAN connection between the instrument and the controlling PC.

In the IR controlled MW experiments (the microwave reactor's own FO sensor is inactive by design) a secondary CEM Discover[®] equipment of the same type was used for simultaneous FO temperature measurement. The IR temperature and applied MW power is recorded through the primary MW reactor, the secondary instrument acts as signal transducer to monitor FO temperature and pressure of the reaction mixture.

The actual power levels in our microwave reactors were tested using the protocol provided by the manufacturer. In a 100 ml round bottom flask 100 ml of distilled water is irradiated for 60 seconds at 300 W fixed power setting. The power is calculated based on the temperature change. All of the values were in the acceptable range.

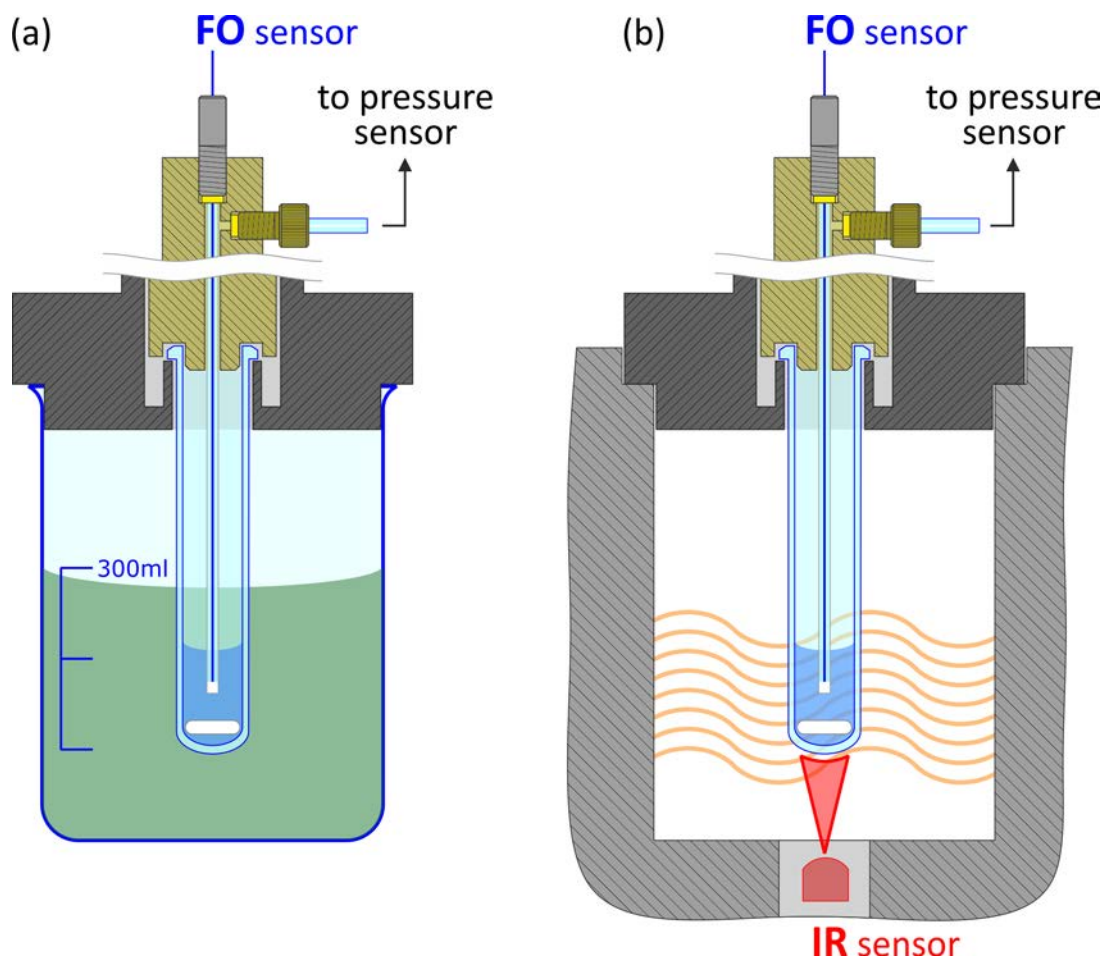


Fig. S1. Experimental set-up (simplified schematic) consisting of oil-bath (a) and microwave (b) heating of geometrically identical reaction vessels.

Calibration of the temperature sensors

The factory calibration of FO sensor was checked by measuring the boiling temperature of a stirred sample of 1-butanol (117°C), N,N-dimethylformamide (153°C) and ethylene glycol (196°C). The calibration was found to be precise (within 2°C) and stable, no modification was needed.

The built-in IR sensor was regularly calibrated. A stirred sample of N,N-dimethylformamide (25 ml) was boiled using continuous microwave irradiation in a 50 ml round-bottom flask under reflux condenser, until stable reflux and constant temperature reading (for at least 5 minutes) was reached. The calibration was adjusted so the boiling temperature is measured as 153°C. The accuracy and linearity of the calibration was checked by measuring the boiling temperature (continuous microwave irradiation while stirring, until reaching stable reflux and constant reading for at least 5 minutes) of 1-butanol (117°C), N,N-dimethylformamide (153°C) and ethylene glycol (196°C). The calibration was found to be precise (within 2°C) and linear in the relevant range.

Harmonized temperature profiles

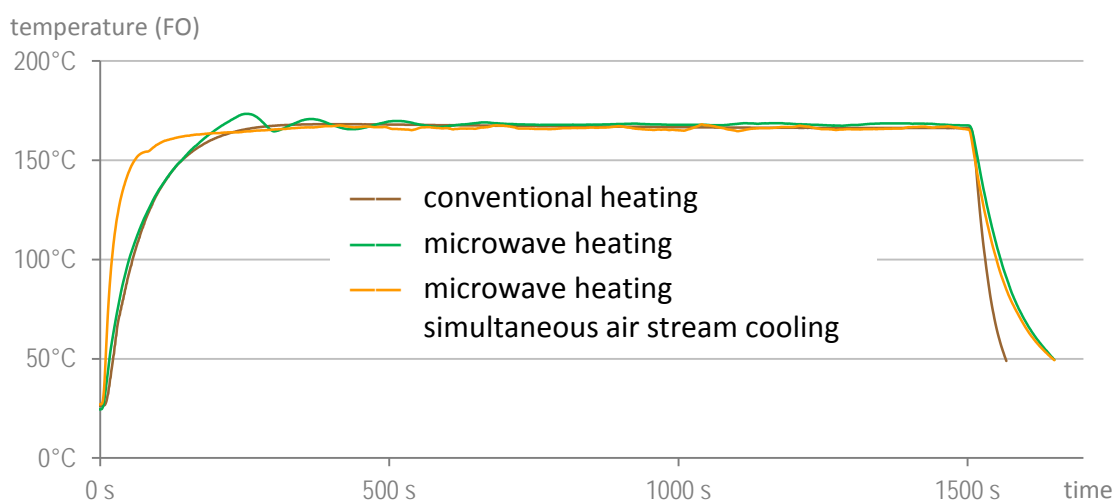


Fig. S2. Comparison of the internal temperature profiles of conventionally and dielectrically heated mixtures of 2-chloropyridine and piperidine. The temperatures were measured during the course of the reaction by the FO sensor.

Conventional heating for 25 min total time using 170°C pre-heated oil bath was conducted, the obtained inner temperature profile (Fig. S2) was recreated in a microwave reactor after extensive experimentation. The set temperature (166°C) was identical to the temperature reached in the oil bath experiment, the power settings leading to the best fit are described in Table S1.

Table S1. Harmonized temperature profiles for the nucleophilic substitution of 2-chloropyridine.

Entry	Heating (control) mode	power setting	mean power (0-1500 s)	heat-up time (to FO 165°C)	mean FO temp. (0-1500 s)	mean IR temp. (0-1500 s)
1	Microwave heating (IR control)	50 W	27 W	134 s	212.3°C	149.8°C
2	Conventional heating (FO monitoring)	–	–	241 s	160.4°C	–
3	MW heating (FO control)	30 W	16 W	194 s	160.2°C	159.6°C
4	MW heating – simultaneous air stream cooling (FO control)	110 W	98 W	270 s	162.9°C	135.9°C

IR controlled microwave heating of incomplete reaction mixtures

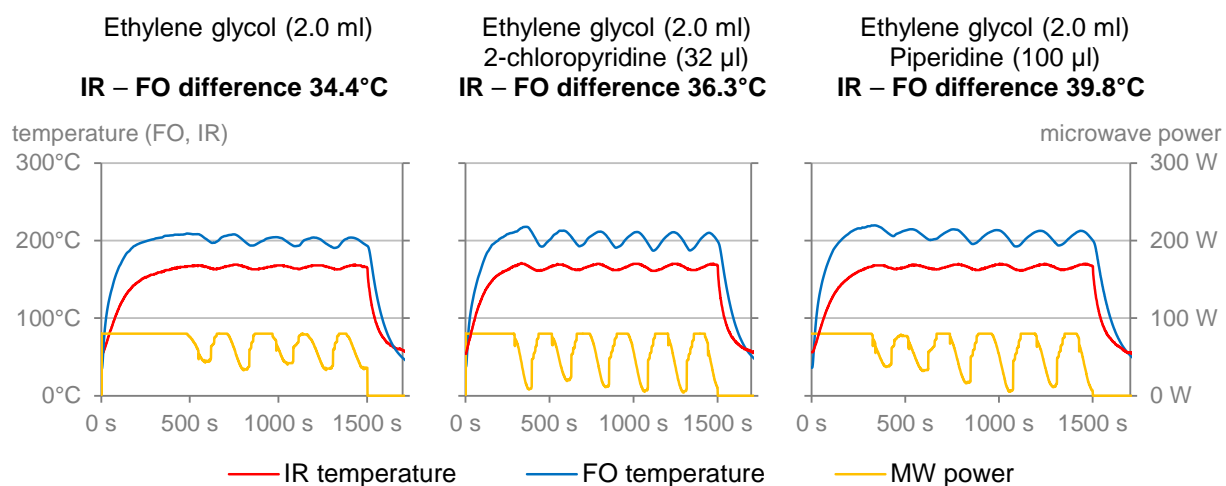


Fig. S3. Difference between IR and FO temperatures in IR controlled microwave heating of incomplete reaction mixtures. (80 W microwave power)

Analysis of the reaction mixtures

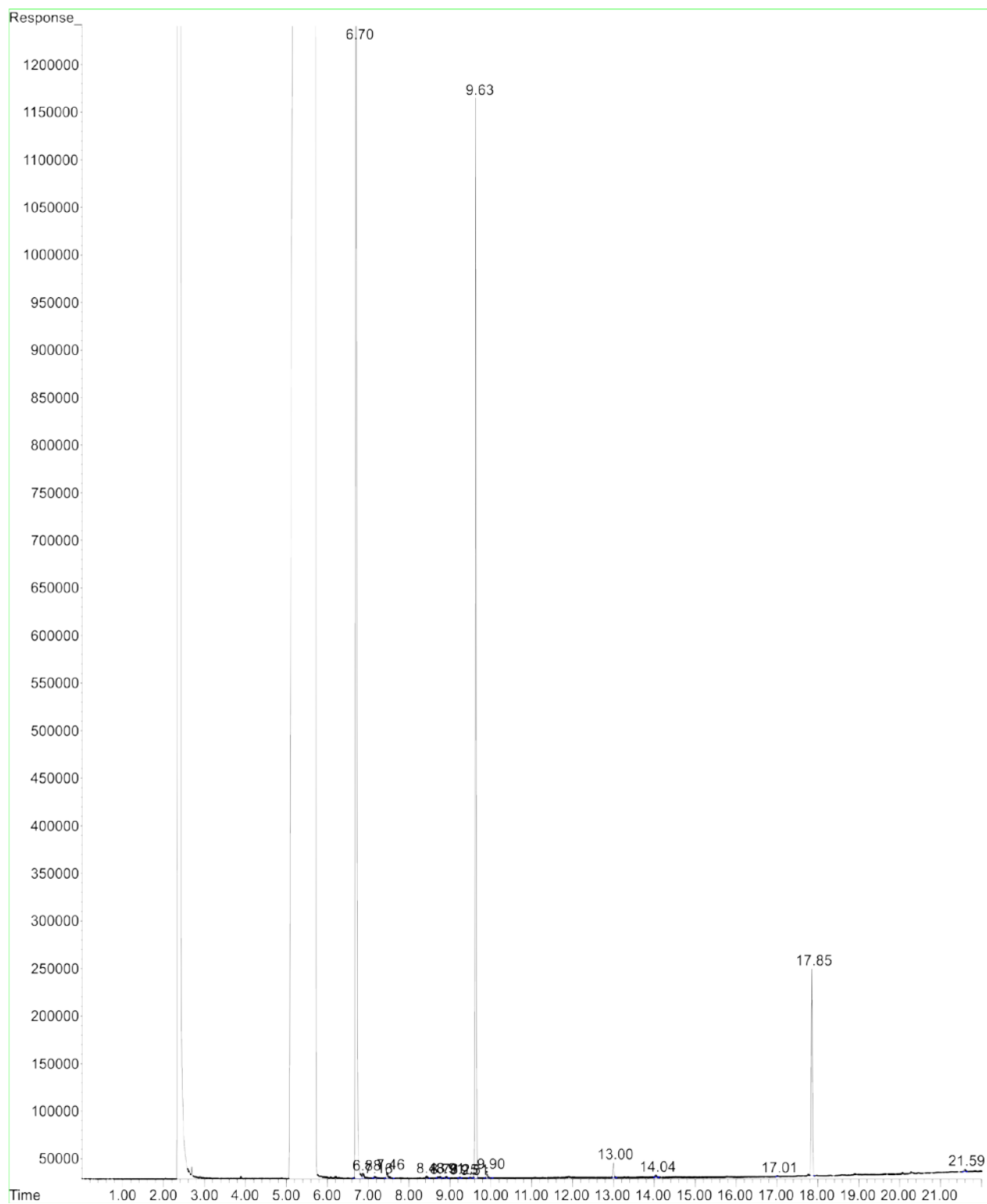


Fig. S4. GC-FID chromatogram of a microwave heated mixture of 2-chloropyridine and piperidine for 25 min at 166°C, showing piperidine (6.70 min), 2-chloropyridine (9.63 min) and the product (17.85 min).

Spectral data of the reaction product (3)

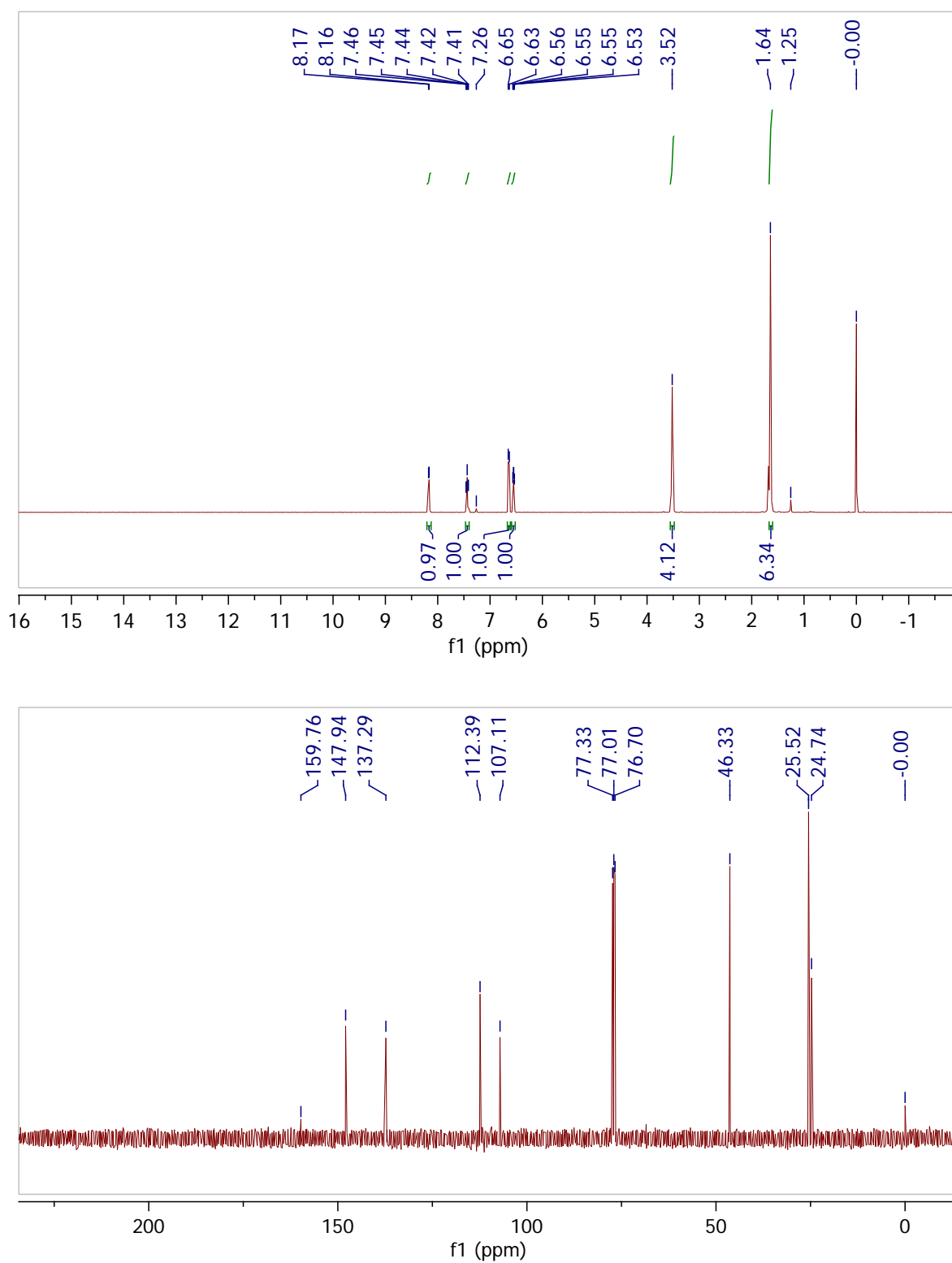


Fig. S5. ¹H-NMR and ¹³C-NMR spectra of a purified sample of the reaction product (3).