Supporting Information

for

The effect of milling frequency on a mechanochemical organic reaction monitored by in situ Raman spectroscopy

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Experimental part

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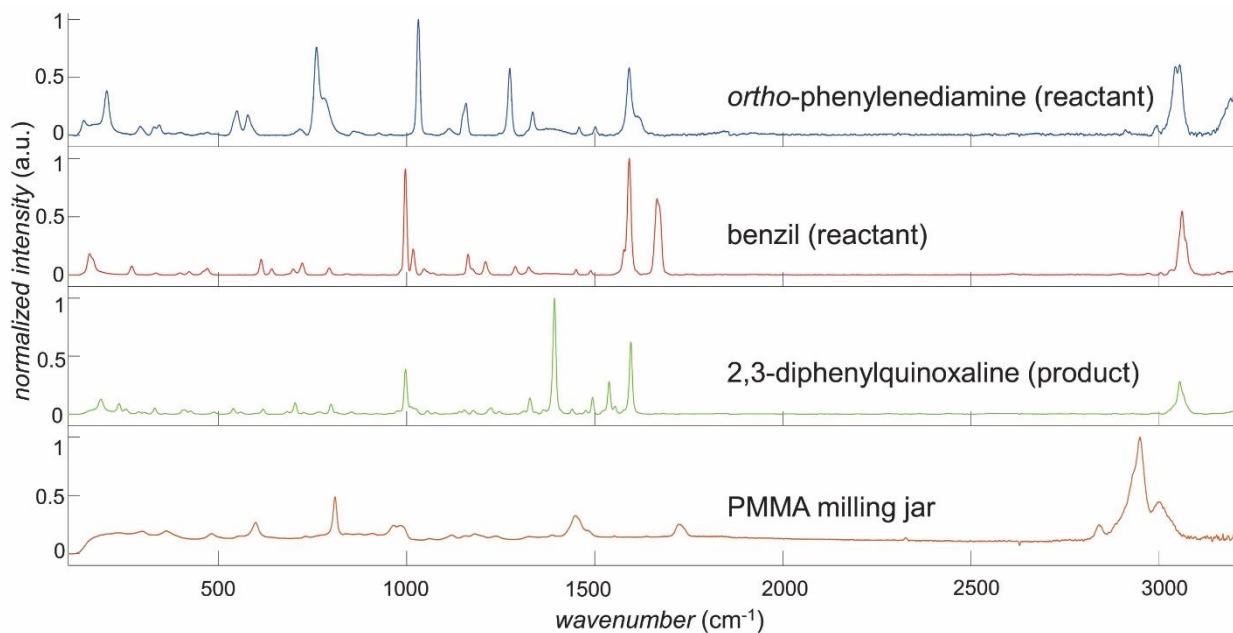
1. Selected Raman spectra of pure components

Figure S1: Relevant Raman spectra (top to bottom): reactant *ortho*-phenylenediamine; reactant benzil; product 2,3-diphenylquinoxaline and an empty PMMA milling jar.

2. Experimental setup

Figure S2: Picture of the experimental setup, showing a 15 mL volume PMMA jar mounted on a milling station of the Retsch MM400 mixer mill and the tip of the Raman spectroscopy probe.
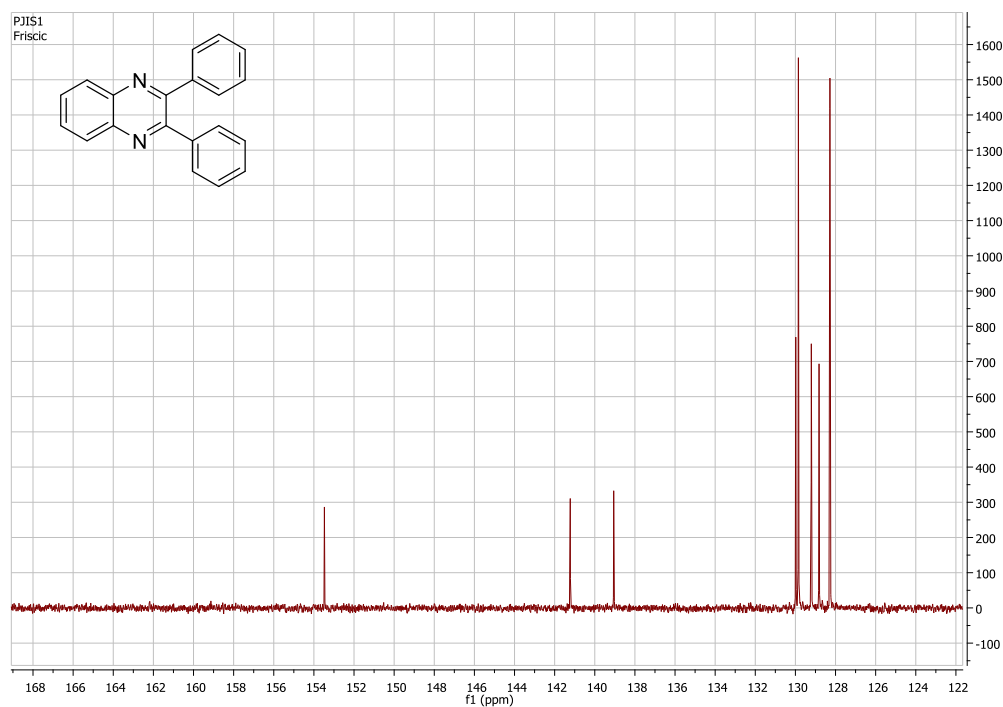
3. Product characterization

Figure S3: ^{1}H NMR spectrum of the crude 2,3-diphenylquinoxaline product obtained by mechanochemical reaction conducted at 30 Hz (30 Hz, Exp. 1), recorded in CDCl$_3$. The spectrum reveals only trace impurities and matches the spectrum previously reported in the *Spectral Database for Organic Compounds (SDBS)*, SDBS No. 32951HSP-48-683.
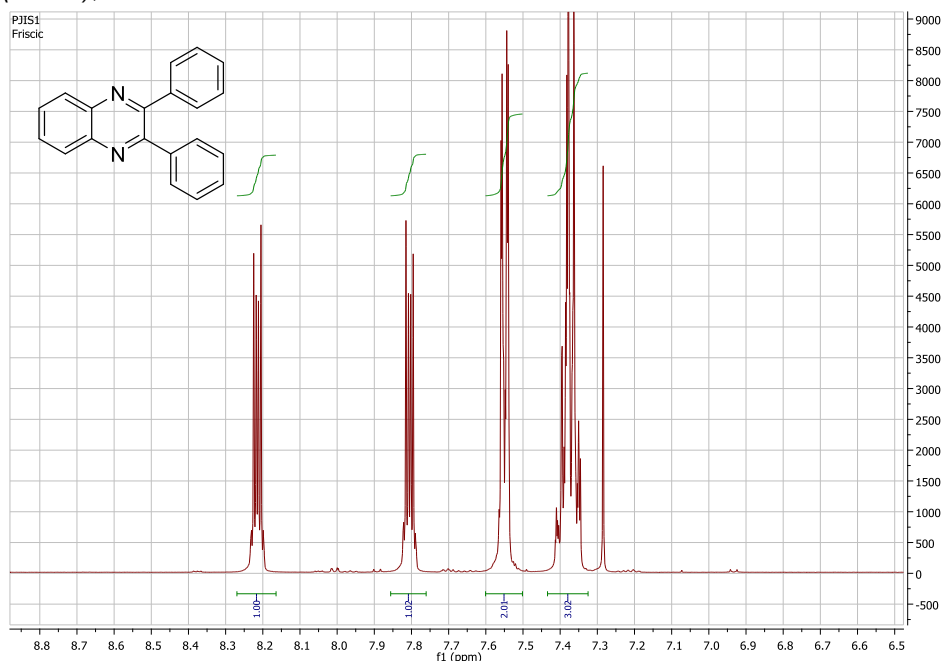

Figure S4: ^{13}C NMR spectrum of the crude 2,3-diphenylquinoxaline product obtained by mechanochemical reaction conducted at 30 Hz (30 Hz, Exp. 1), recorded in CDCl$_3$. The spectrum reveals only trace impurities and matches the spectrum previously reported in the *Spectral Database for Organic Compounds (SDBS)*, SDBS No. 32951CDS-10-500
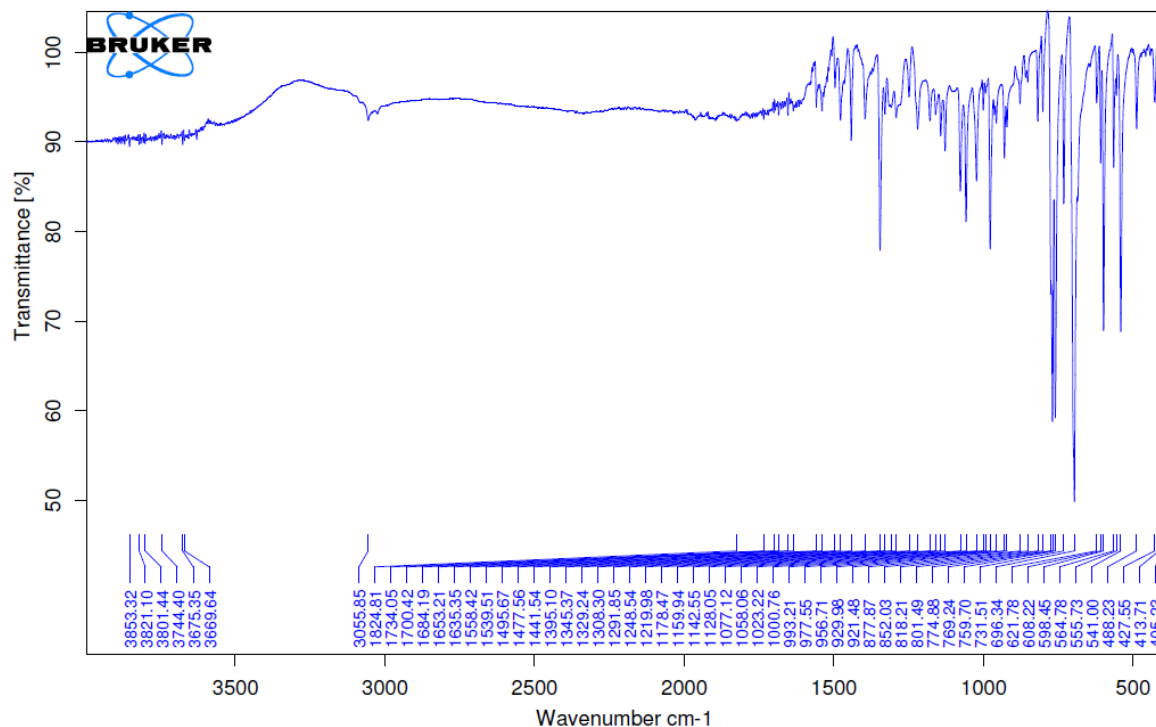
Figure S5: Fourier-transform infrared attenuated total reflectance (FTIR-ATR) spectrum of the crude 2,3-diphenylquinoxaline product obtained by mechanochemical reaction conducted at 30 Hz (30 Hz, Exp. 1). The spectrum matches the spectrum previously reported in the *Spectral Database for Organic Compounds (SDBS)*, SDBS No. 32951 IR-NIDA-74153.
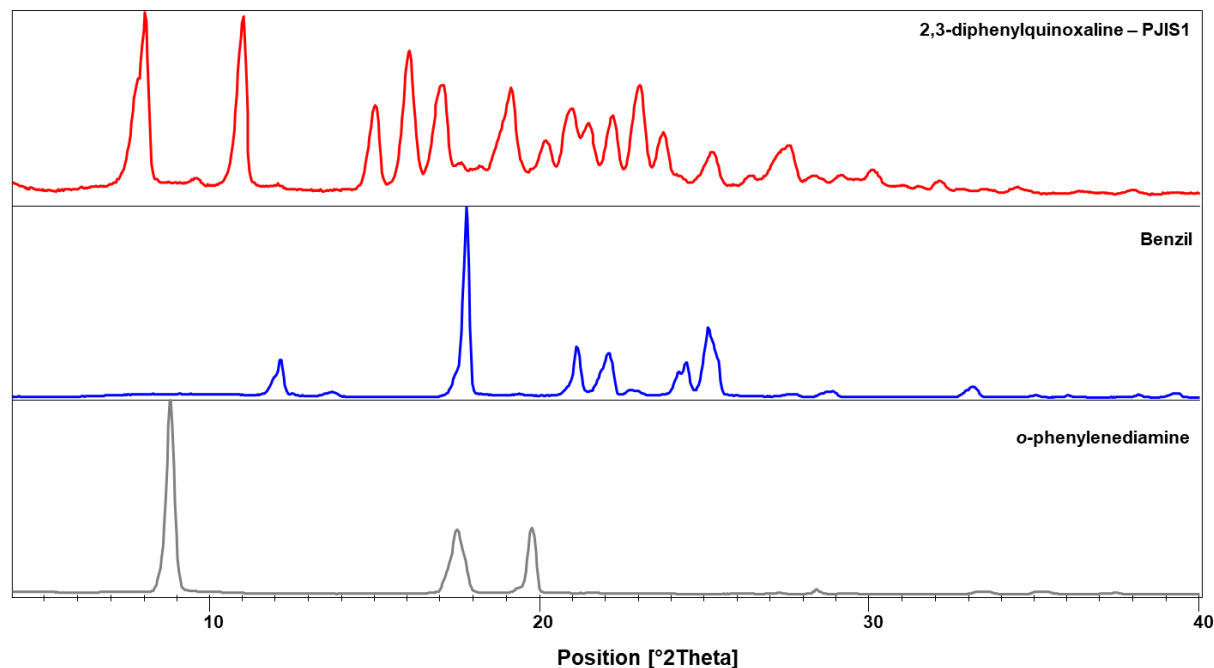

Figure S6: Example powder X-ray diffraction patterns for the mechanochemical synthesis of 2,3-diphenylquinoxaline (top to bottom): the crude product of the reaction conducted by ball milling at 30 Hz (30 Hz, Exp. 1); benzil reactant and reactant *ortho*-phenylenediamine.

Table S1: Reaction conversions, based on integration of ^{1}H NMR spectra of crude milling products. If starting material could not be detected, conversion is listed as 99+%

Reaction Number	Frequency (Hz) and Experiment #	Conversion (%)
1	30, Exp. 1	99+
2	30, Exp. 2	99+
3	30, Exp. 3	99+
4	27.5, Exp. 1	99+
5	27.5, Exp. 2	99+
6	27.5, Exp. 3	97.0
7	25, Exp. 1	99+
8	25, Exp. 2	98.0
9	25, Exp. 3	99+
10	22.5, Exp. 1	99+
11	22.5, Exp. 2	99+
12	22.5, Exp. 3	99+
13	20, Exp. 1	79.5
14	20, Exp. 2	74.5
15	20, Exp. 3	83.0

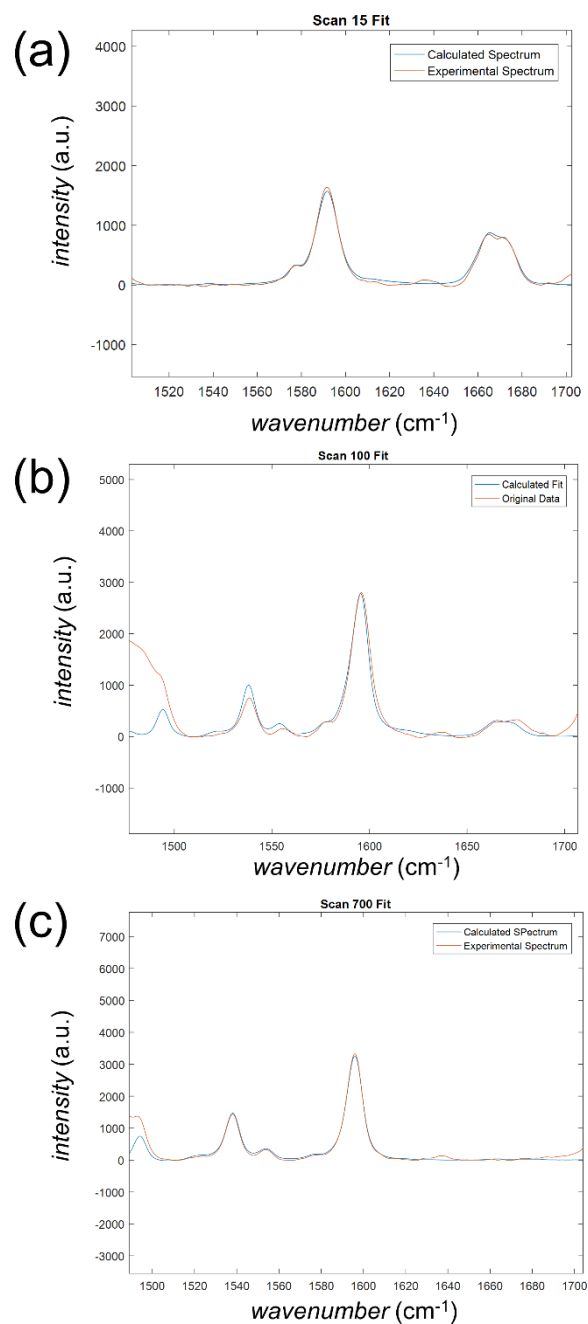## 4) Spectroscopic data and fitting plots for all experiments

Figure S7: Comparison of experimental and calculated spectra for Experiment 1, 30 Hz (the complete dataset and residuals for this experiment are presented in the article, main paper): (a) scan #15 (after 75 seconds milling); (b) scan #100 (after 500 seconds milling) and (c) scan #700 (after 3500 seconds milling).
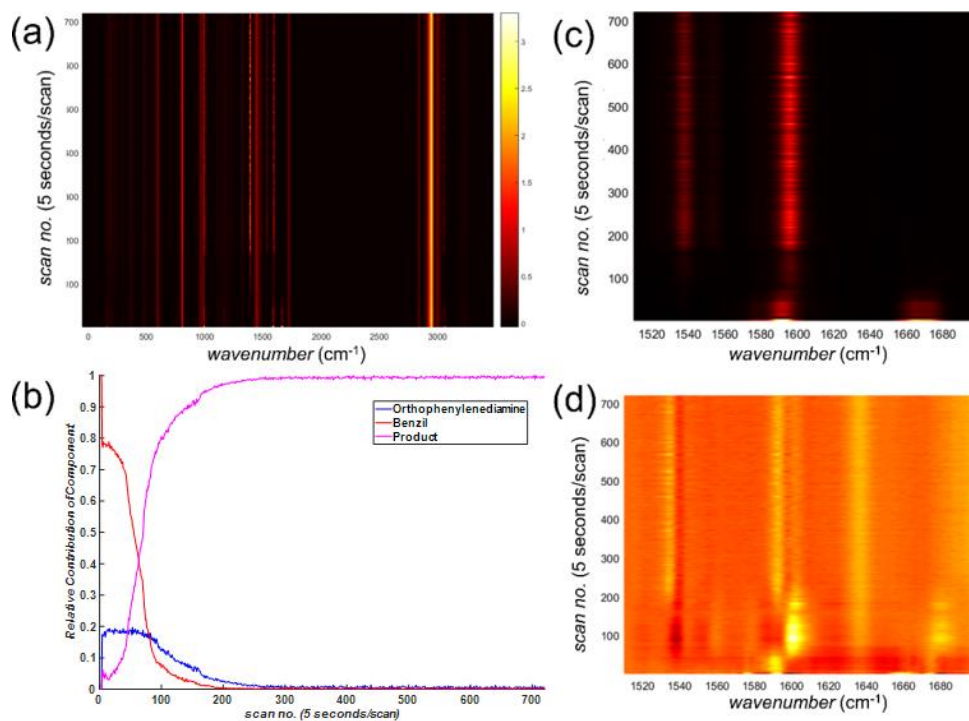
Figure S8: Data for Experiment 2, 30 Hz: (a) the entire time-resolved Raman spectrum for the second experiments conducted by milling at 30 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
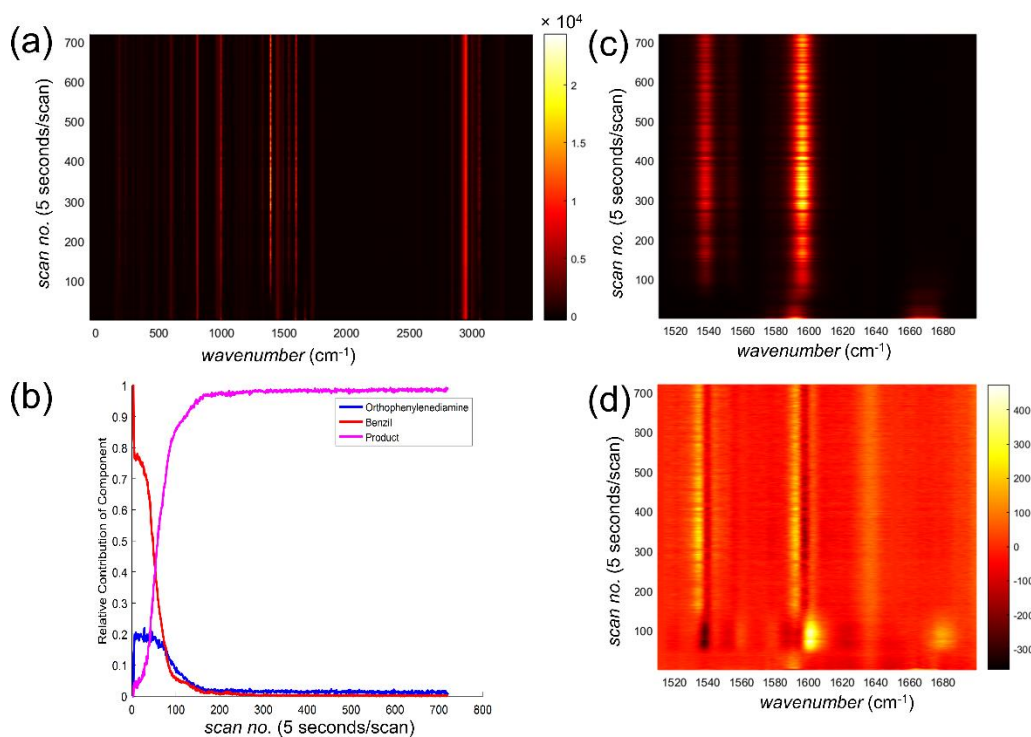

Figure S9: Data for Experiment 3, 30 Hz: (a) the entire time-resolved Raman spectrum for the third experiment conducted by milling at 30 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
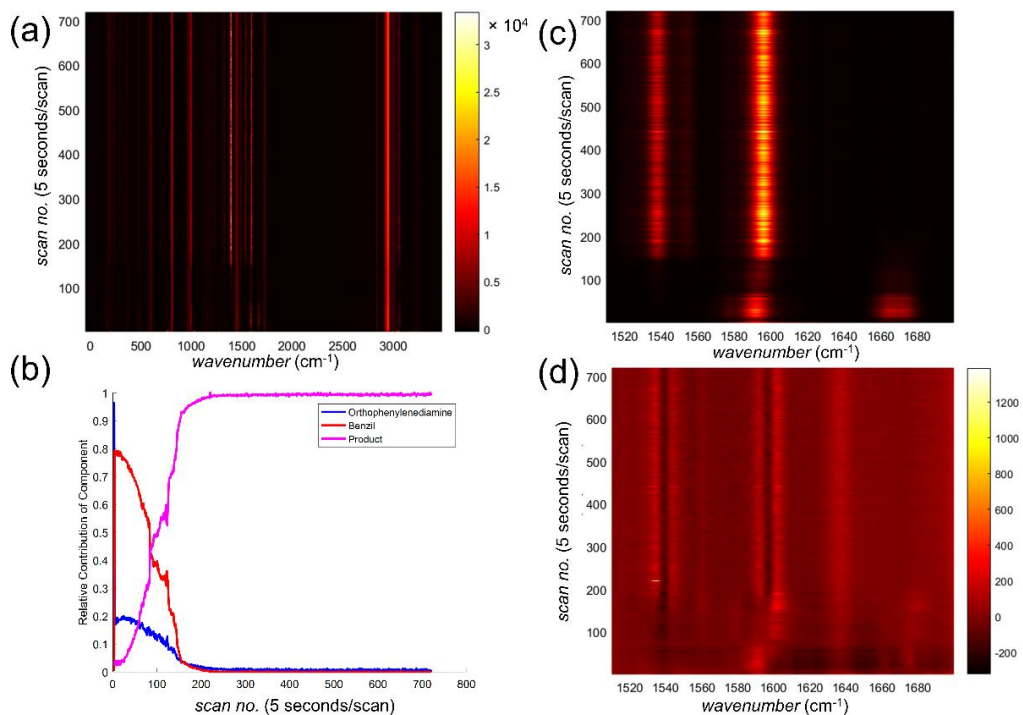
Figure S10: Data for Experiment 1, 27.5 Hz: (a) the entire time-resolved Raman spectrum for the first experiment conducted by milling at 27.5 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
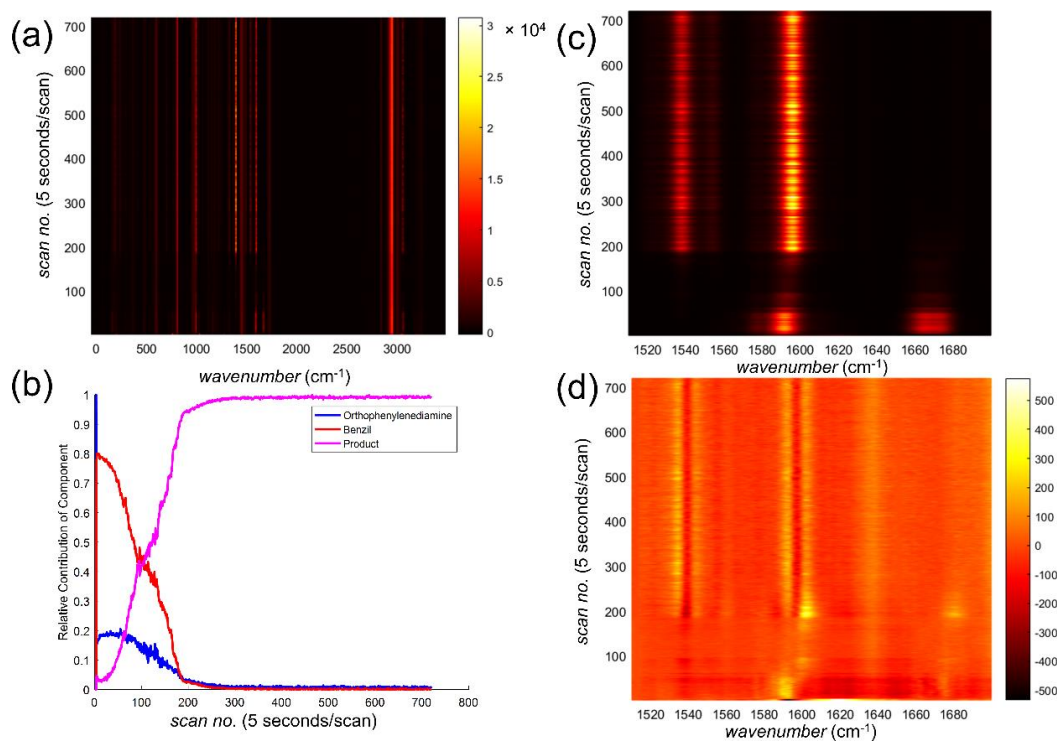

Figure S11: Data for Experiment 2, 27.5 Hz: (a) the entire time-resolved Raman spectrum for the second experiment conducted by milling at 27.5 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
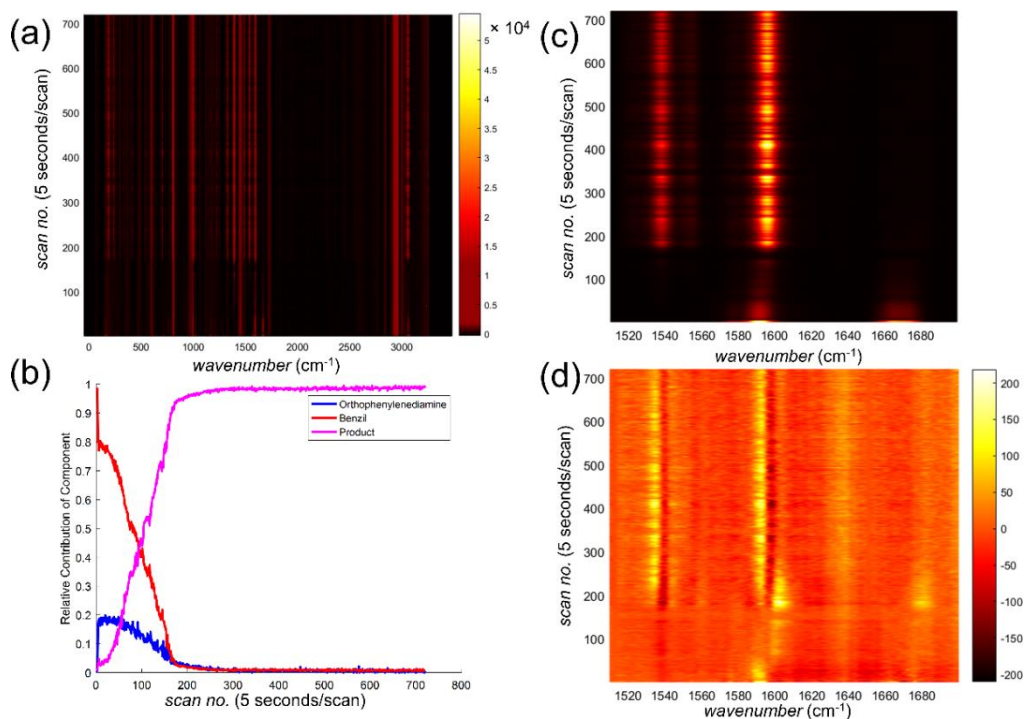
Figure S12: Data for Experiment 3, 27.5 Hz: (a) the entire time-resolved Raman spectrum for the third experiment conducted by milling at 27.5 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
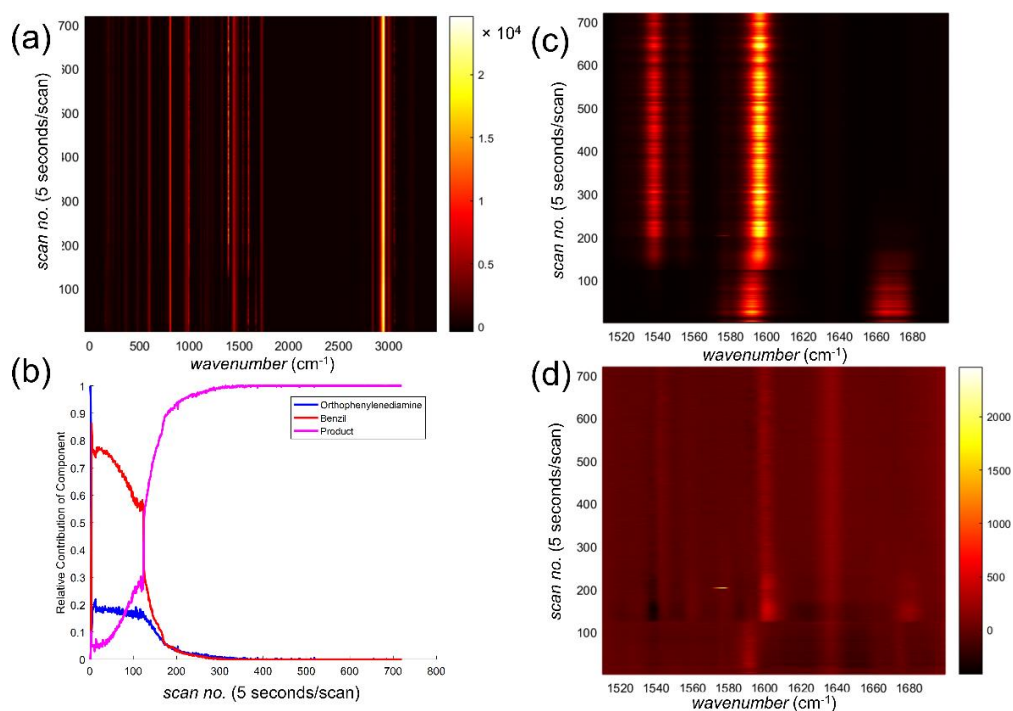

Figure S13: Data for Experiment 1, 25 Hz: (a) the entire time-resolved Raman spectrum for the first experiment conducted by milling at 25 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
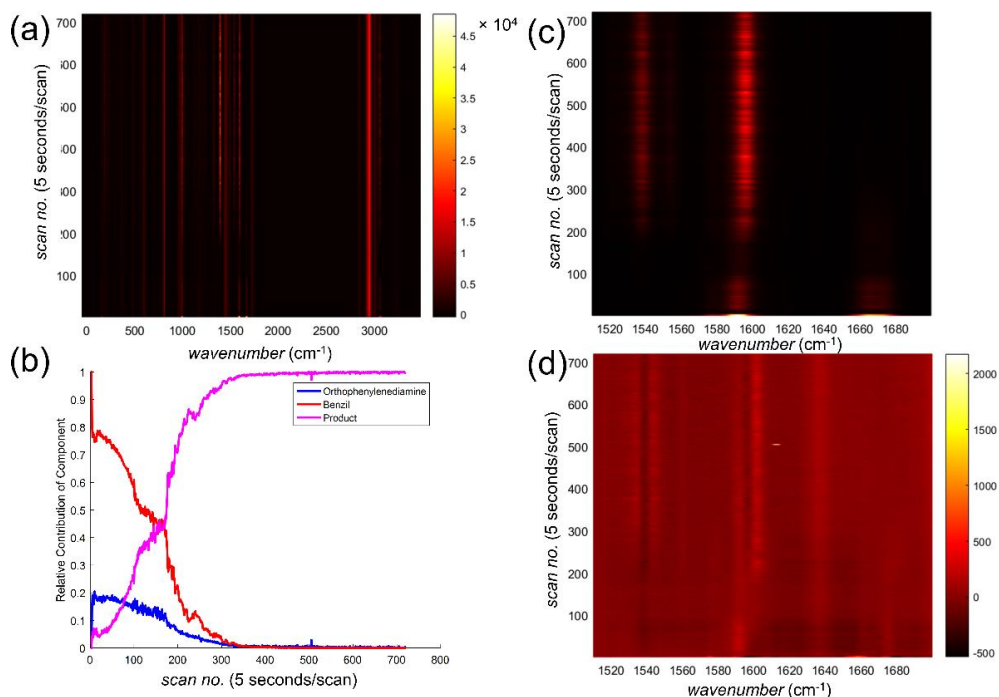
Figure S14: Data for Experiment 2, 25 Hz: (a) the entire time-resolved Raman spectrum for the second experiment conducted by milling at 25 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
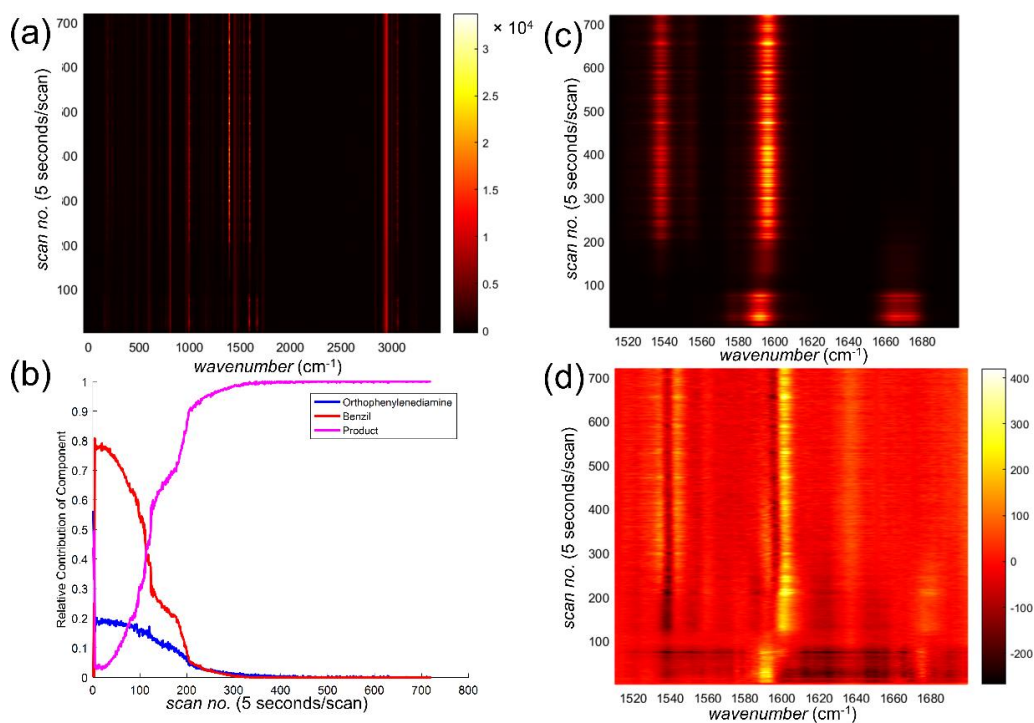

Figure S15: Data for Experiment 3, 25 Hz: (a) the entire time-resolved Raman spectrum for the third experiment conducted by milling at 25 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
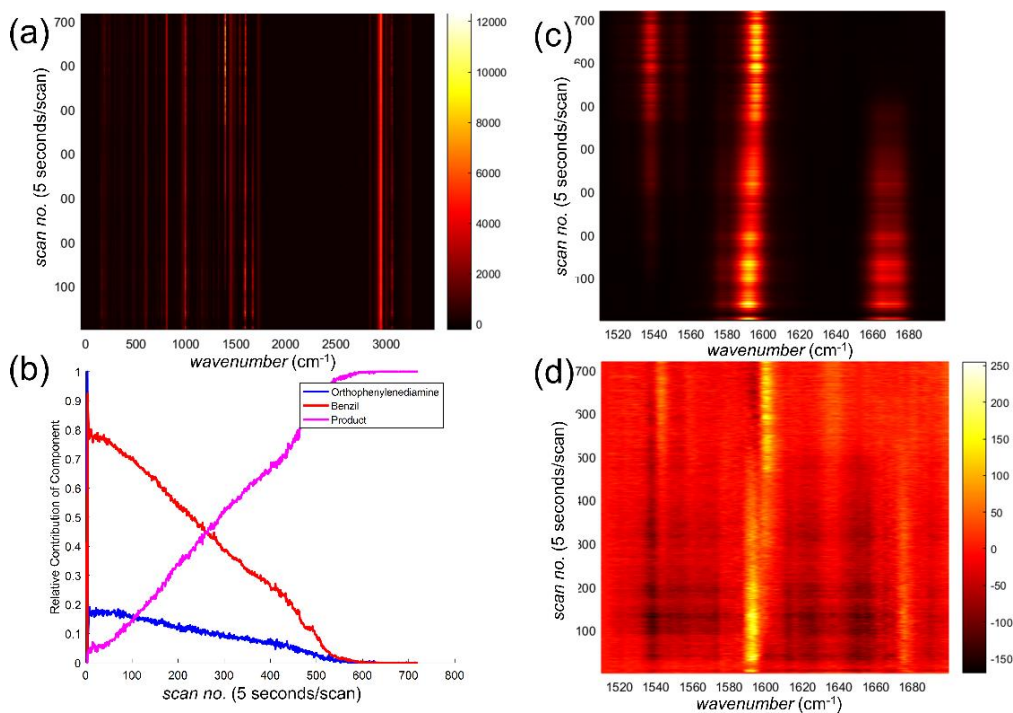
Figure S16: Data for Experiment 1, 22.5 Hz: (a) the entire time-resolved Raman spectrum for the first experiment conducted by milling at 22.5 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
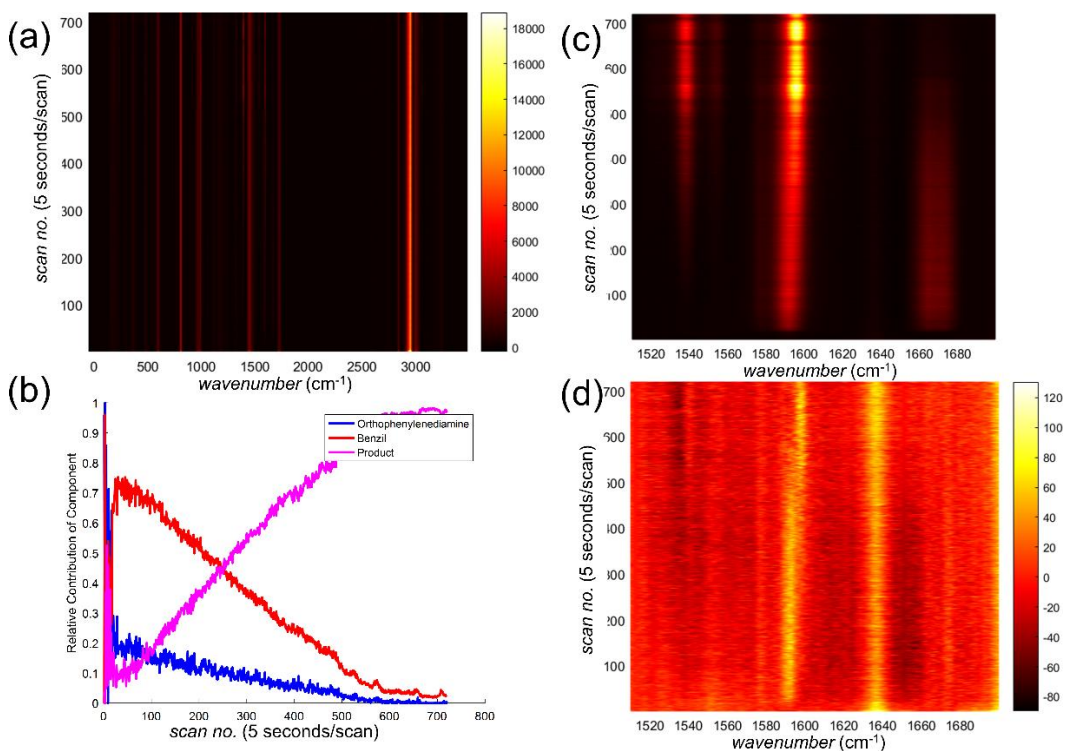

Figure S17: Data for Experiment 2, 22.5 Hz: (a) the entire time-resolved Raman spectrum for the second experiment conducted by milling at 22.5 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
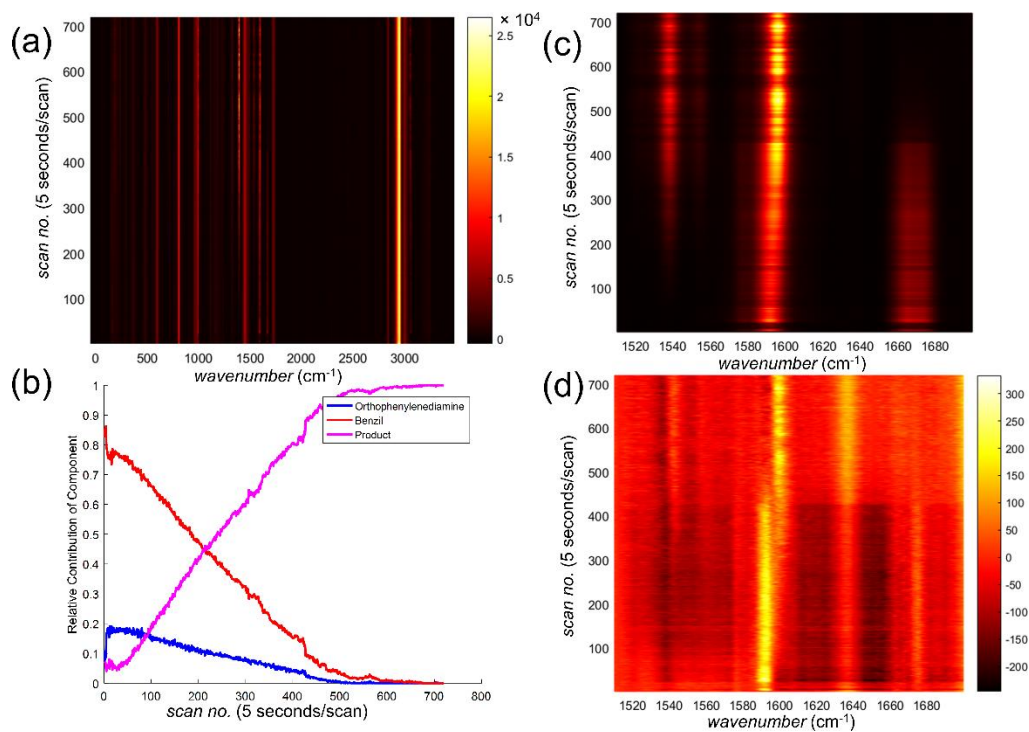
Figure S18: Data for Experiment 3, 22.5 Hz: (a) the entire time-resolved Raman spectrum for the third experiment conducted by milling at 22.5 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
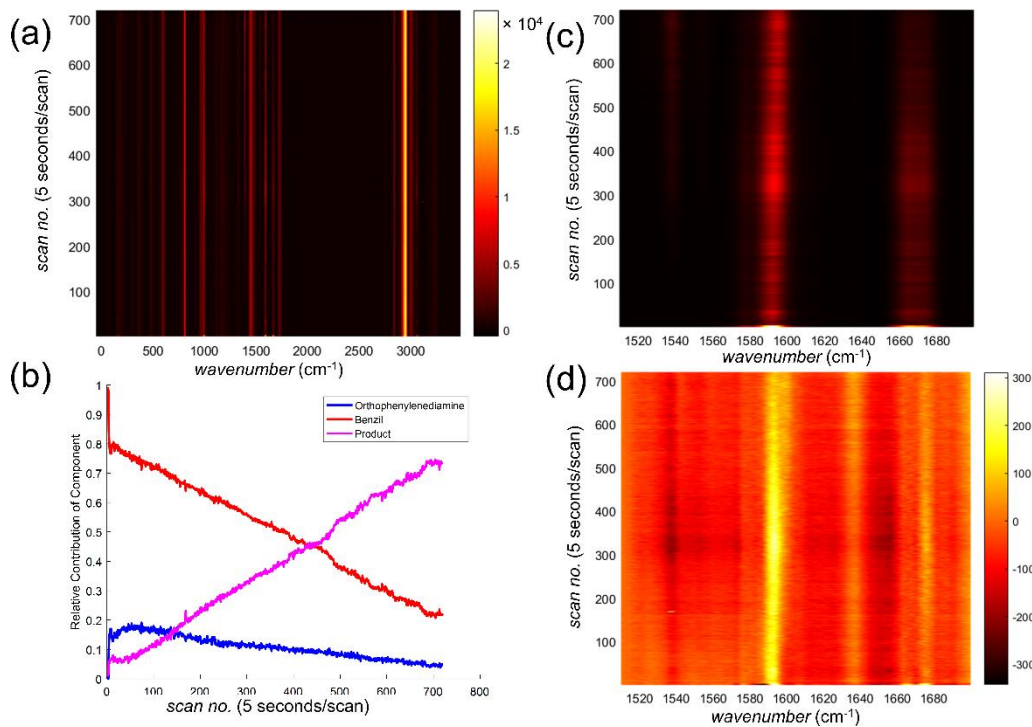

Figure S19: Data for Experiment 1, 20 Hz: (a) the entire time-resolved Raman spectrum for the first experiment conducted by milling at 20 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
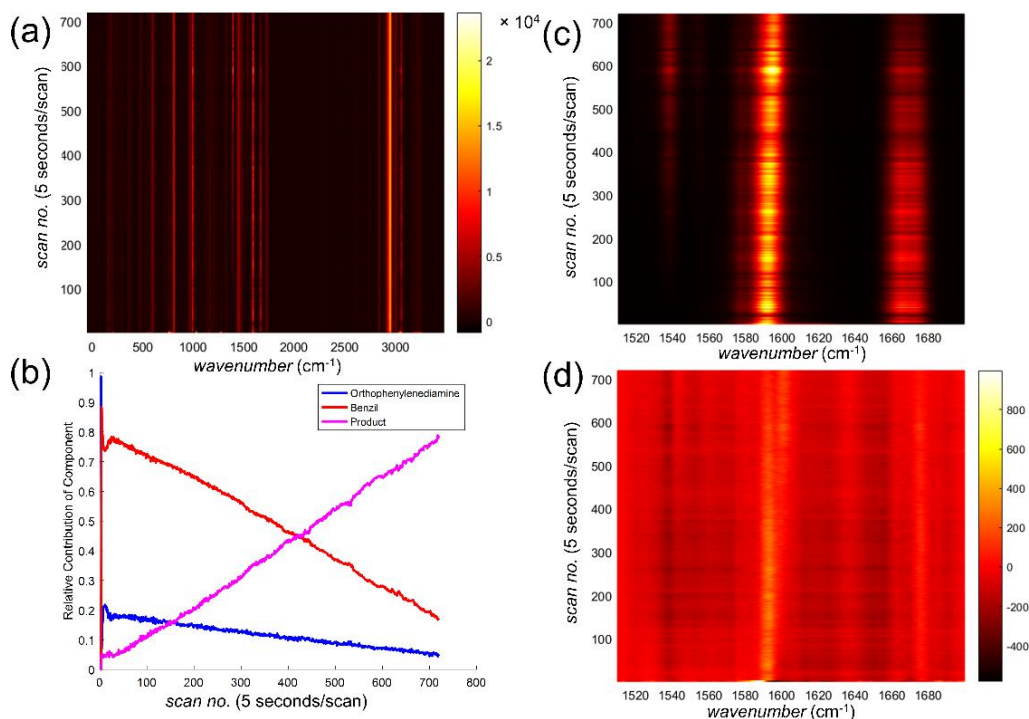
Figure S20: Data for Experiment 2, 20 Hz: (a) the entire time-resolved Raman spectrum for the second experiment conducted by milling at 20 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.
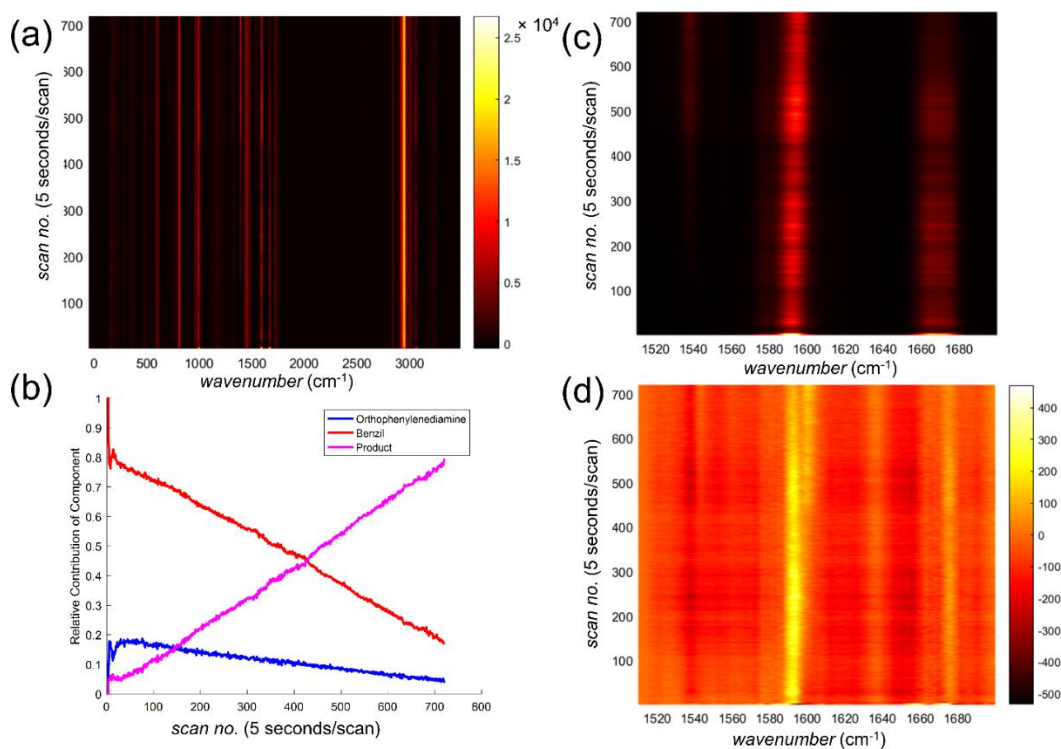

Figure S21: Data for Experiment 3, 20 Hz: (a) the entire time-resolved Raman spectrum for the third experiment conducted by milling at 20 Hz; (b) the associated time-dependent change in spectral contributions of the product (purple) and the two reactants (red and blue); (c) section of the spectrum selected for least-squares fitting and (d) the final residual spectrum.