1. Experimental

1.1. Chemicals, Reagents and Columns

DMSO (Catalog#51779, GC-headspace tested, ≥99.9%), DMF (Catalog#51781, GC-headspace tested, ≥99.9%), 3-phenoxylbenzyl chloride (Catalog# 590932, ≥97%) and 3-phenoxybenzaldehyde (Catalog# 191752, ≥98%) were purchased from Sigma-Aldrich. Acetonitrile (Catalog# 015-4, HPLC grade) was purchased from Burdick&Jackson. Water for HPLC analysis was in house generated MilliQ water. DMS (Catalog# 22949, ≥99%) was purchased from Alfa Aesar and phosphoric acid (Catalog# PX0996-6, 85%) was purchased from EMD. Permethrin API was provided by Merial Inc. GC columns were purchased through VWR and HPLC columns were purchased from Waters.

1.2. Instrumentation and Data Acquisition

The GC system was an Agilent GC 7890 equipped with a FID detector and an Agilent 1888 Headspace auto sampler. HPLC system was an Agilent 1200 equipped with diode array detector. Data acquisition and processing were accomplished using Empower® 3 software.

1.3. Chromatographic Conditions and sample preparation

1.3.1. GC conditions, sample preparation and calculation

Column used for GC was a DB-624 column (30 m x 0.53 mm, 3.0 μm film thickness) and oven program was 40 °C hold for 10 minutes, then 50 °C/minute to 200 °C and hold for 5 minutes. Split ratio was 1:5 and flow rate was 4.5 mL/min, inlet temperature was 140 °C and detector was flame ionization detector (FID). Headspace loop temperature was 140 °C, transfer line temperature was 160 °C, vial pressure was 13 psi, headspace vial was 20 mL and injection volume was 1 mL. When kinetics study were conducted at different temperatures, only headspace oven temperature and heating time changed and other parameters remained unchanged.

For GC analysis of PMN sample in DMSO, about 200 mg of PMN was added into a 20 mL headspace GC vial, pipetted 5.0 mL DMSO or DMF into the vial, capped the vial and crimped it immediately.

For GC analysis of PMN sample spiked with DMS, about 200 mg of PMN was added into a 20 mL headspace GC vial, pipetted 5.0 mL of DMS external reference standard solution into the vial, capped the vial and crimped it immediately.

For neat PMN sample GC analysis, about 200 mg of PMN was added into a 20 mL headspace GC vial, capped the vial and crimped it immediately.

For GC analysis of DMSO or DMF blank, pipetted 5.0 mL of the solvent into a 20 mL headspace GC vial, capped the vial and crimped it immediately.

DMS external reference standard solution preparation:
Dissolved and diluted DMS in DMSO to reach about 10 µg/mL (equivalent to about 1.6×10^{-4} mol/L).

For quantitation of DMS when PHOCl was heated in DMSO:
Prepared 3-phenoxybenzyl chloride solution in DMSO to reach about 16 µg/mL (about 7×10^{-5} mol/L) and pipetted 5.0 mL of this solution into a 20 mL headspace GC vial, capped the vial and crimped it immediately.
Before and after the GC analysis of the sample solution, two GC analyses of the DMS external reference standard solutions were performed as following: pipetted 5.0 mL of the DMS external reference standard solution into a 20 mL headspace GC vial and crimped it immediately. The vial was heated for the same time and at the same temperature as the sample solution in the headspace oven before injected to the GC for analysis.
The DMS concentration in the sample solution was calculated using the formula below:

$$\text{DMS concentration} = \frac{Au}{As} \times Cs$$

Au = Peak area of DMS in the sample solution

As = Average peak area of DMS of the two external reference standard injections
Cs = Concentration of DMS in the external reference standard solution

1.3.2. HPLC conditions and sample preparation for PMN heating at 130°C

Column was a Waters XBridge C18 with 150 mm x 4.6 mm and particle size was 3.5µm. Mobile phase A (MA) was 0.05% (v/v) of phosphoric acid in water and mobile phase B (MB) was acetonitrile. Diluent was acetonitrile/water 60/40 (v/v). Column temperature was 30°C. Detection wavelength was 215 nm and injection volume was 20 µL. Gradient elution was conducted: 30% MB at initial hold for 1 minute and then MB increased from 30% to 100% from 1 minute to 40 minutes. The mobile phase combination was returned to initial and equilibrated for 5 minutes before next injection.

Analytical procedure for heating PMN at 130 °C: Dissolved 4 g of PMN in 100 mL DMSO. To five 20 mL headspace GC vials, pipetted 5.0 mL of the solution into each vial, capped the vials and crimped them immediately. These vials were heated at 130°C for 10, 30, 60, 120 and 240 minutes in the headspace oven. These vials were cooled down to room temperature and then diluted with diluent (acetonitrile/water 60/40 (v/v)) to reach 0.2 mg/mL. The PMN solution in DMSO at initial without heating was also diluted by the diluent to reach 0.2 mg/mL. All these solutions were analyzed by the HPLC conditions described above. Peak areas of each impurities and PMN were listed in Table 1. Overlaid HPLC Chromatograms and peak area% changed are listed in Figure 3 and Table 1 of the manuscript.

1.3.3. HPLC conditions and sample preparation for kinetics study

Column and all parameters were the same as HPLC conditions for PMN analysis except an isocratic elution was conducted with MA: MB as 35:65 (v/v) and run time as 8 minutes.

Prepared 3-phenoxybenzyl chloride solution in DMSO to reach about 16 µg/mL (about 7 $x10^{-5}$ mol/L) and pipetted 5.0 mL each of this solution into 20 mL headspace GC vials, capped the vials and crimped them immediately. Each vial was heated in the headspace oven for designed times and temperature before removed from the oven and cooled to room temperature. 4 mL of the solution in each vial was diluted to 20 mL with diluent (about 3 µg/mL of initial 3-

phenoxybenzyl chloride concentration, equivalent to about $1.5x10^{-5}$ mol/L) for further HPLC analysis.

External reference standard solution preparation:

Dissolved 3-phenoxylbenzyl chloride and 3-phenoxybenzaldehyde in diluent to reach about 3 μg/mL (equivalent to about $1.5x10^{-5}$ mol/L for 3-phenoxylbenzyl chloride and $1.7x10^{-5}$ mol/L for 3-phenoxybenzaldehyde) each as the external standard solution.

Before and after the HPLC analysis of the sample solution, two HPLC analyses of the external reference standard solutions were performed.

The 3-phenoxylbenzyl chloride concentration in the DMSO solution was calculated using the formula below:

Concentration in DMSO solution = Au/As×Cs×Du

Au = Peak area of 3-phenoxylbenzyl chloride in the sample solution

As = Average peak area of 3-phenoxylbenzyl chloride of the two external reference standard injections

Cs = Concentration of 3-phenoxylbenzyl chloride in the external reference standard solution

Du = Dilution factor of DMSO solution which is 5

2. Chromatograms and Results

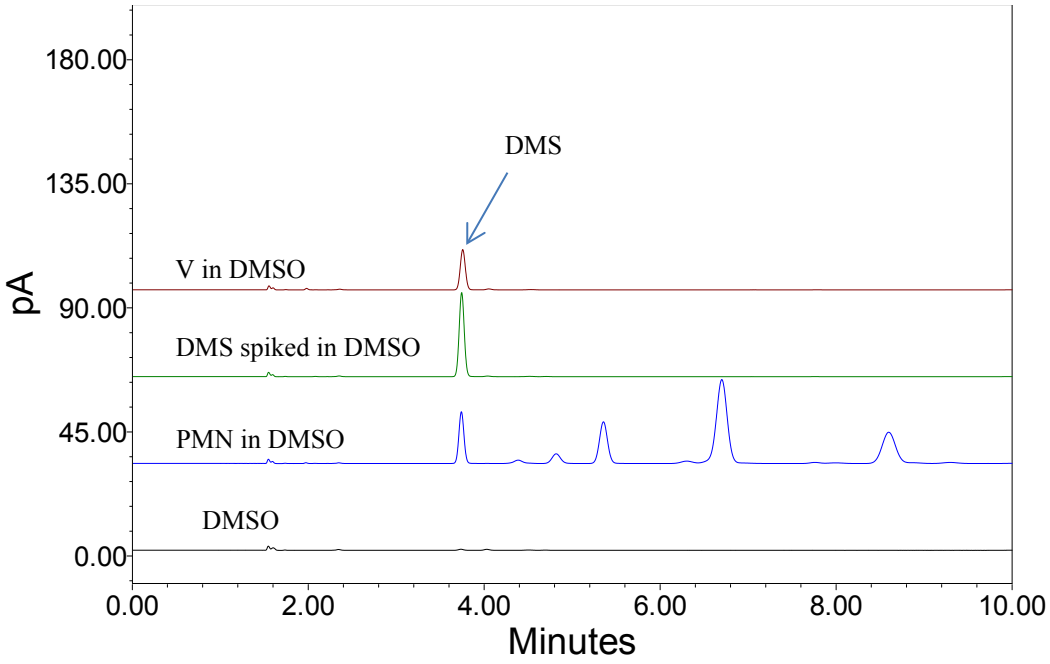

Figure 1. . Overlaid GC Chromatograms From Bottom to Top: DMSO, PMN in DMSO, DMS spiked in DMSO and 3-phenoxybenzyl chloride (V) in DMSO . (All samples were heated at 130°C for 30 minutes in headpace GC vials prior to GC analysis).

Note: In DMSO, there was a small peak at the retention time of DMS and this peak was confirmed to be DMS by GC-MS. The concentration of DMS in DMSO was below the quantitation limit of the headspace GC method ($<1.6 \times 10^{-6}$ mol/L).

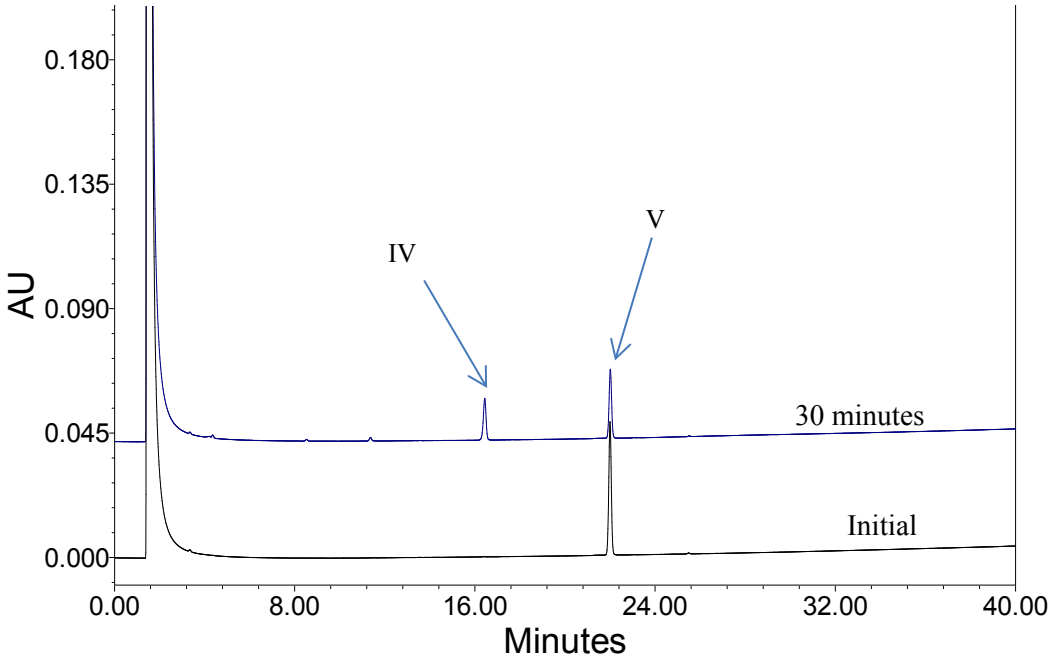

Figure 2. . Overlaid HPLC Chromatograms Bottom: 3-phenoxybenzyl chloride (V) in DMSO before heating and Top: V in DMSO heated at 130 °C for 30 minutes

Table 1. Peak Area by HPLC after PMN Heated in DMSO at 130°C

Time, min	Peak area of each compounds by HPLC								
	Ia	Ib	IIa	IIb	III	IV	V	VI	Other
initial	11985604	8308982	21913	7174	48269	21779	29530	7469	90525
10	11978076	8302194	20856	7117	49172	26412	28169	7288	89098
30	11897783	8243610	20475	7196	49158	31836	21946	7275	88202
60	12091278	8376696	21909	7114	51051	36372	16850	7199	90707
120	12015903	8329642	20502	7021	51305	40571	10671	7243	87929
240	12000608	8321418	20659	7079	52906	44484	6651	7270	87538

Note: Peak area percentages of each compound are listed in table 1 of the paper

Table 2. Logarithmic Concentrations of 3-Phenoxybenzyl Chloride (V) in DMSO After Heating at Different Temperatures

Temperature (K)	Ln (concentration of V, mol/L) at each time point				
	900s	1800s	3600s	7200s	10800s
343	-9.678	-9.700	-9.734	-9.778	-9.831
	-9.678	-9.701	-9.732	-9.777	-9.829
353	-9.702	-9.734	-9.789	-9.899	-9.931
	-9.702	-9.736	-9.791	-9.898	-9.933
363	-9.734	-9.782	-9.859	-9.960	-10.025
	-9.734	-9.786	-9.862	-9.961	-10.023
373	-9.799	-9.881	-9.925	-10.062	-10.151
	-9.807	-9.866	-9.925	-10.061	-10.160
383	-9.863	-9.969	-10.056	-10.250	-10.336
	-9.865	-9.971	-10.051	-10.248	-10.340
393	-9.920	-10.047	-10.212	-10.418	-10.557
	-9.919	-10.046	-10.213	-10.425	-10.559
403	-10.035	-10.190	-10.453	-10.829	-11.123
	-10.013	-10.192	-10.452	-10.830	-11.122

Note: Linear regression analysis was performed for logarithmic concentrations (mol/L) of V vs time (second) at each temperature. Slope of each linear curve was k (s^{-1}) at each temperature.

Table 3. Decrease of 3-Phenoxybenzyl Chloride (V) and Formation of 3-Phenoxybenzaldehyde (IV) and DMS after V was heated in DMSO at 130 °C

Time, min	3-Phenoxybenzyl chloride		DMS		3-Phenoxybenzaldehyde	
	μg/mL	10^{-5} mol/L	μg/mL	10^{-5} mol/L	μg/mL	10^{-5} mol/L
15	9.695	4.433	1.438	2.314	4.047	2.042
30	8.203	3.751	1.970	3.171	5.488	2.769
60	6.315	2.888	2.513	4.043	7.088	3.576
120	4.332	1.981	3.097	4.983	8.788	4.433
180	3.231	1.477	3.464	5.575	9.729	4.908

Note: DMS concentrations were determined by GC using external standard of DMS; IV and V concentrations were determined by HPLC using external standard of IV and V.