Thermal Stability Analysis for Major Reaction Components of Ohira-Bestmann Reagent

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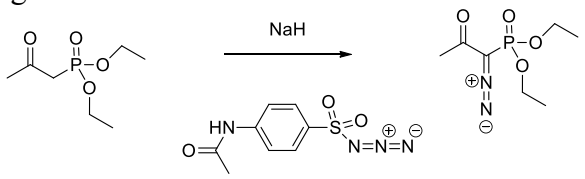
The purpose of this study is to screen thermal stability of starting material, reagent and product in the following reaction:



Summary of Findings and Recommendations

- The starting material diethyl(2-oxopropyl)phosphonate exhibits exothermic events near 246°C (ΔH= -376 J/g) and 278°C (ΔH= -376 J/g).
- 4-acetamidobenzenesulfonyl azide exhibits an exothermic event near 116°C (ΔH= -1280 J/g) and additional exothermic events near 211°C (ΔH= -17 J/g) and 297°C (ΔH= -145 J/g).
- The product diethyl(1-diazo-2-oxopropyl)phosphonate exhibits exothermic events near 86°C (ΔH= -689 J/g), 226°C (ΔH= -107 J/g) and 276°C (ΔH= -32 J/g).
- In the event that pH is lowered, hydrazoic acid may be formed. The hydrazoic acid is unstable and may decompose violently.

Testing Results

- DSC test results are summarized below:

Compound	ΔH (J/g)	Range (°C)
Diethyl(2-oxopropyl)phosphonate, Oakwood lot 079617N05H, CAS 1067-71-7	-376	246-276
	+37(endo)	276-278
	-659	278-347
4-acetamidobenzenesulfonyl azide, Oakwood lot 450489R06R, CAS 2158-14-7	+91(endo)	95-116
	-1280	116-204
	-17	211-247
	-145	297-336
Product, Diethyl(1-diazo-2-oxopropyl)phosphonate, lot 15062986-0761	-689	86-210
	-107	226-268
	+50(endo)	268-276
	-32	276-295

- The azide reagent, 4-acetamidobenzenesulfonyl azide, exhibits an exothermic event detected near 116°C (ΔH= -1280 J/g).
- The liquid form product, diethyl(1-diazo-2-oxopropyl)phosphonate, exhibits exothermic events near 86°C (ΔH= -689 J/g). The safe handing temperature of the product should be ~100ºC below the onset temperature, giving the safety margin for the data obtained using DSC. (Distillation may not be performed without further investigation).
- In the event that pH is lowered, hydrazoic acid may be formed. The hydrazoic acid is unstable and may decompose violently. It has a boiling point of 36°C and a lower explosion limit (LEL) of 10% in nitrogen. The hydrazoic acid may react with metals or organic materials to form unstable metal azides or other organic azides. To prevent the formation of explosive atmosphere in the reactor, nitrogen may need to be flowing through the reactor to keep the hydrazoic acid vapor concentration below 25% of the LEL.

DSC Results

Differential Scanning Calorimetry (DSC) results were acquired in this study with a Mettler Toledo Differential Scanning Calorimeter. Samples were first sealed in gold plated high pressure metal cell or glass cell and heated in the DSC furnace, typically from 0°C to 400°C at 1 – 10°C/min.

Thermal stability of the starting materials, intermediates, and final product was examined by DSC. The results are summarized in Table 1 and the following figures.[1]

Table 1: DSC Results

Compound	Mass (mg)	Test Number	Figure	ΔH (J/g)	Range (°C)
Diethyl(2-oxopropyl)phosphonate, Oakwood lot 079617N05H, CAS 1067-71-7	17.77	23003	1	-376	246-276
				+37(endo)	276-278
				-659	278-347
4-acetamidobenzenesulfonyl azide, Oakwood lot 450489R06R, CAS 2158-14-7	8.85	23001	2	+91(endo)	95-116
				-1280	116-204
				-17	211-247
				-145	297-336
Product, Diethyl(1-diazo-2-oxopropyl)phosphonate, lot 15062986-0761	11.45	23002	3	-689	86-210
				-107	226-268
				+50(endo)	268-276
				-32	276-295

Figure 1: DSC Results for Diethyl(2-oxopropyl)phosphonate

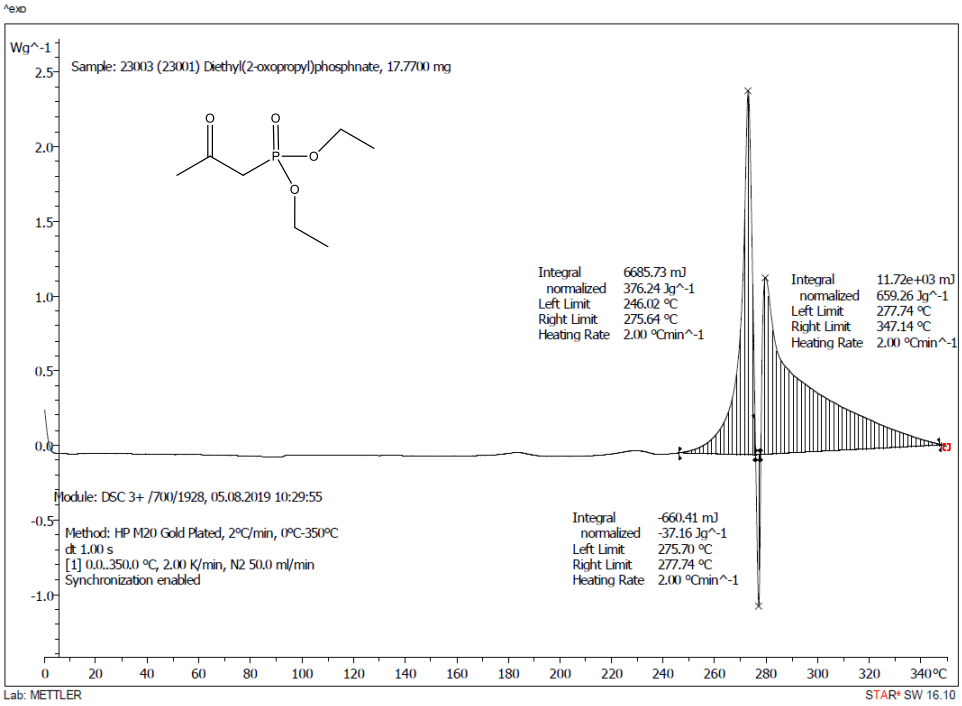


Figure 2: DSC Results for 4-acetamidobenzenesulfonyl azide

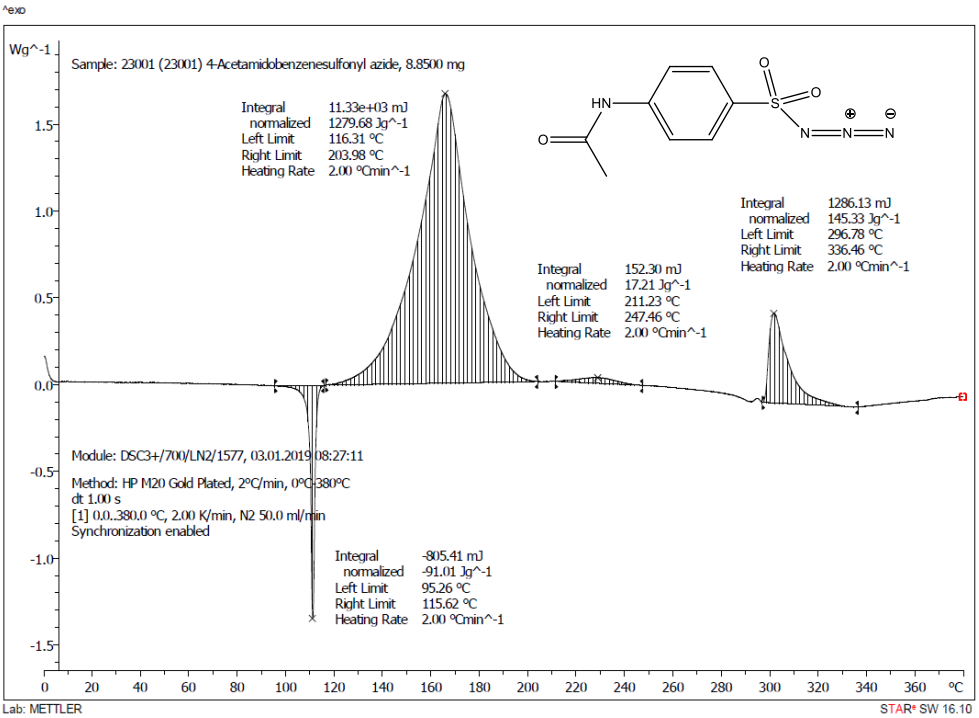


Figure 3: DSC Results for Diethyl(1-diazo-2-oxopropyl)phosphonate