

The Nitration of 8-Methylquinoxalines in Mixed Acid

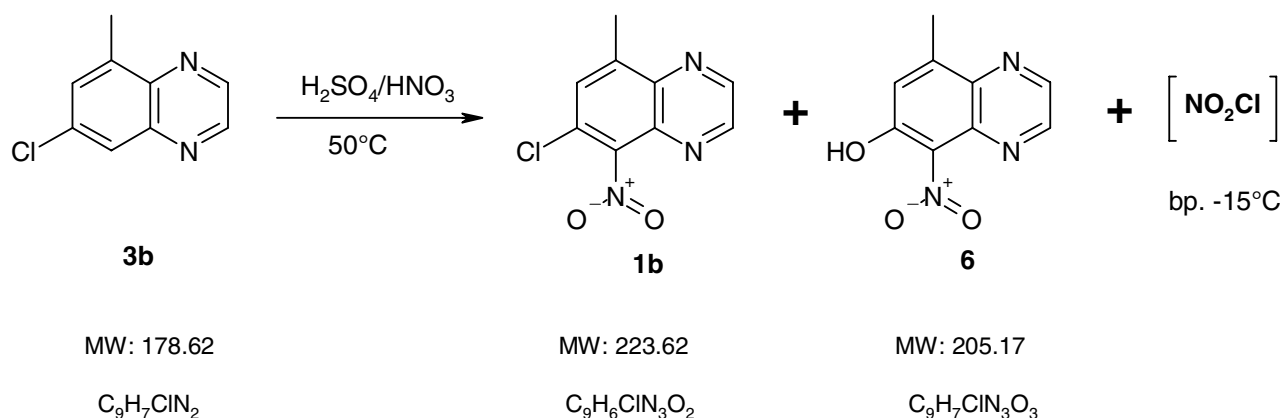
Wolfgang Marterer,^{*§} Walter Prikoszovich,[§] Jacques Wiss,[§] Mahavir Prashad[#]

[§] Novartis Pharma AG, Chemical and Analytical Development, CH-4002 Basel, Switzerland.

[#] Novartis Institute for Biomedical Research, Chemical and Analytical Development, East Hannover, NJ 07936, USA.

Supporting Information. Some selected charts of the calorimetric (RC1 Mettler) and thermostability (DSC Mettler TA 8000; heating program 4°C/min) measurements are shown in this supplement to exemplify the conclusions discussed in the manuscript for the nitration of **3b** -> **1b** + **6**.

Reaction scheme:



Experimental set-up as described in experimental section: a) Dissolve **3a** in sulfuric acid (salt formation). b) Add freshly prepared, cold mixed acid in a two staged addition profile at 50°C. c) After

completed reaction, hydrolyse by inverse addition of the reaction mass to cold water (containing sulfaminic acid to degrade the excess nitric acid to N_2O and N_2).

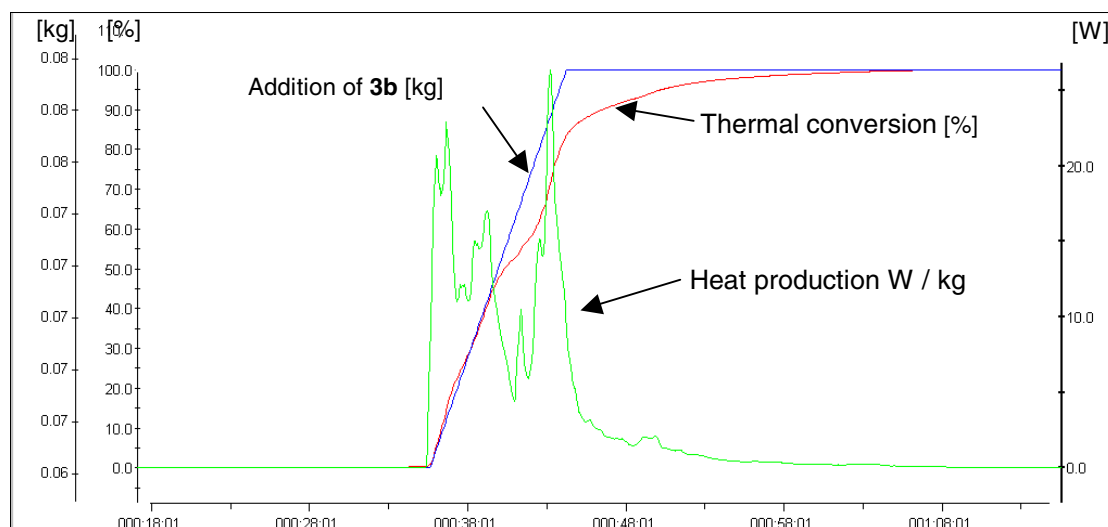


Chart 1. Reaction calorimetry in Mettler RC 1: Dissolving of **3b** in sulfuric acid at 25°C.

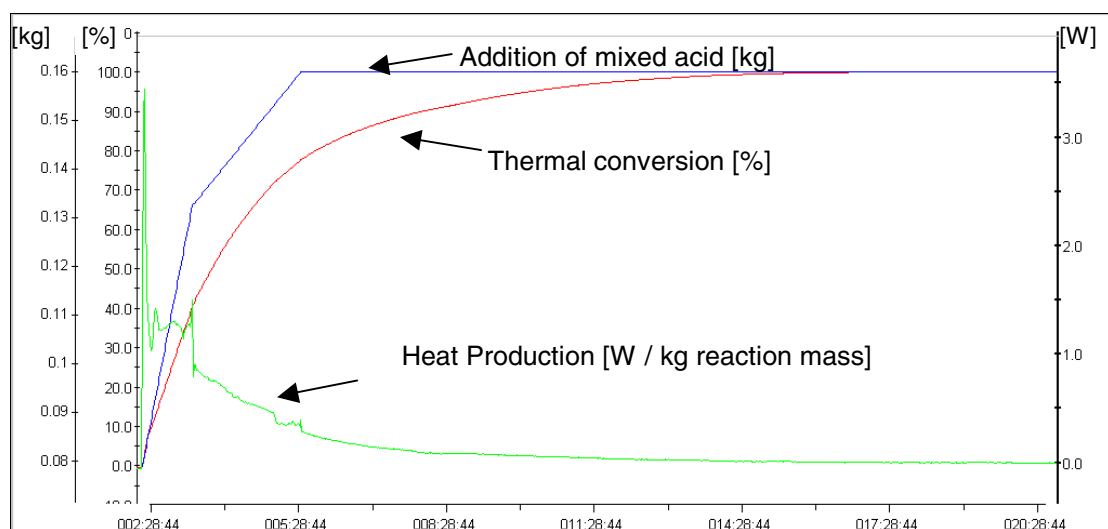


Chart 2. Reaction calorimetry in Mettler RC 1: Two staged addition of mixed acid (2/3 of the amount in 1h; 1/3 in 2 h) to the sulfuric acid solution of **3b** at 50°C.

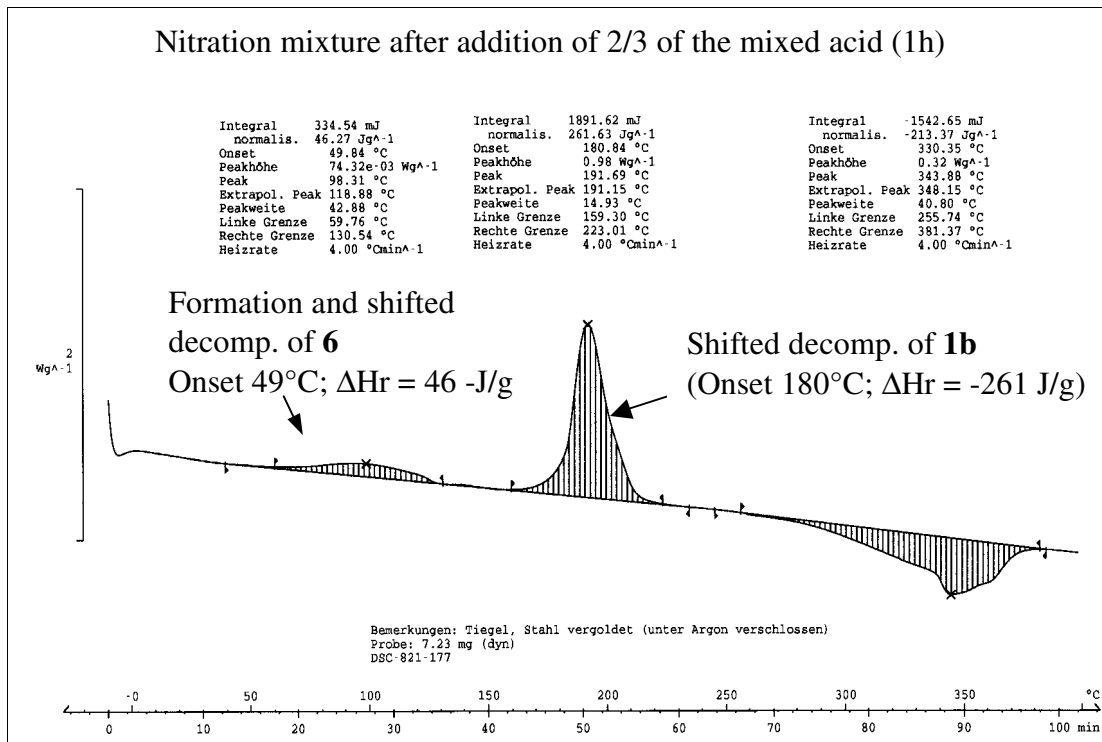


Chart 3. Dynamic DSC thermostability test of the nitration mixture after 2/3 of mixed acid is added at 50°C (1 h).

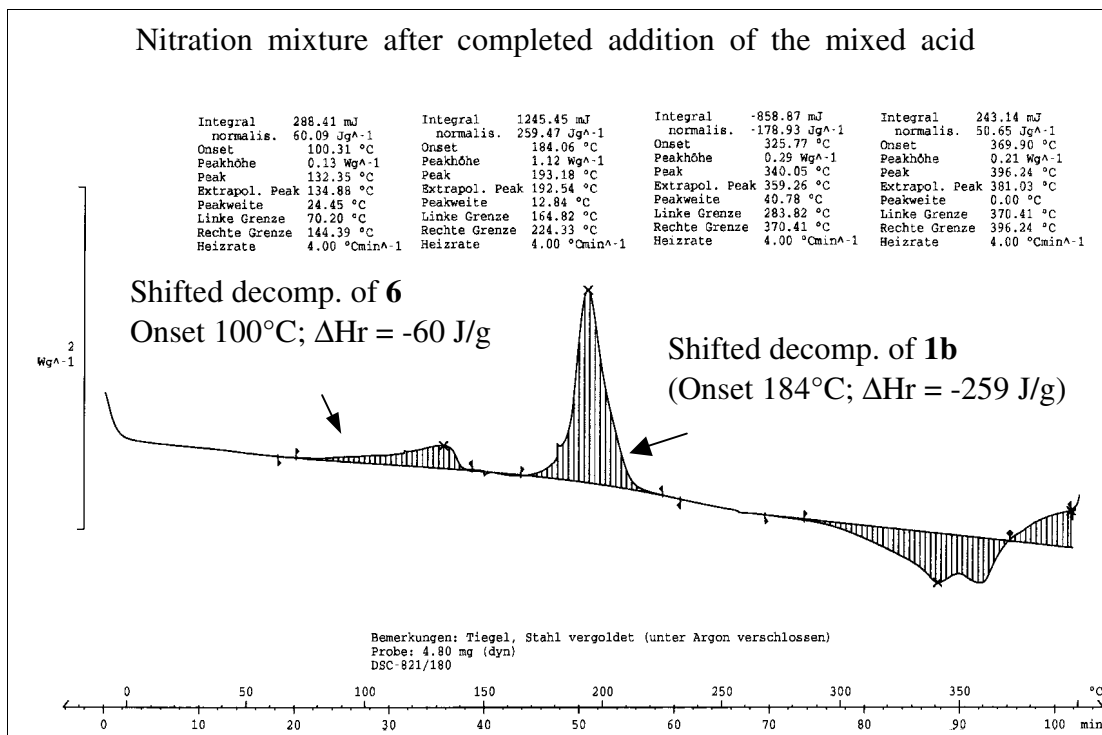


Chart 4. Dynamic DSC thermostability test of the nitration mixture after completed addition of mixed acid at 50°C (3 h).

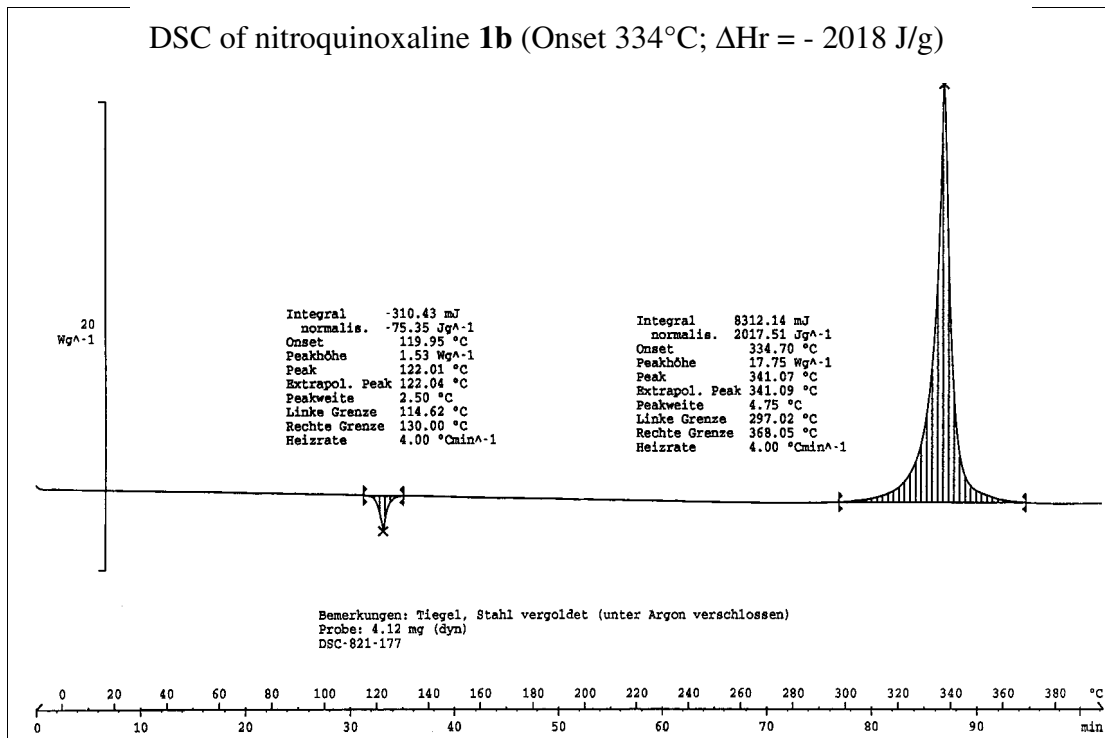


Chart 5. Dynamic DSC thermostability test of crystallized product 1b

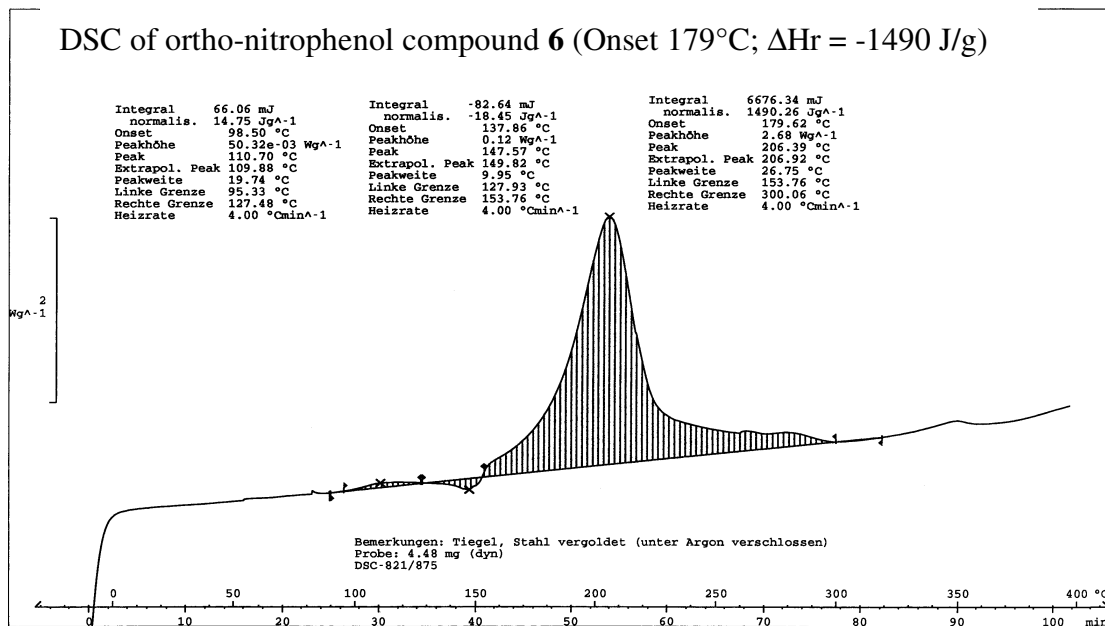


Chart 6. Dynamic DSC thermostability test of by-product 6