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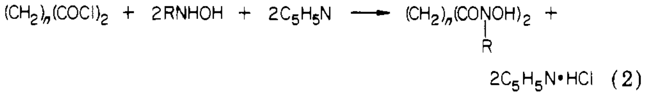
$$(CH_2)_n(COOEt)_2 + 2NH_2OH + 2NaOEt \longrightarrow$$

$$(CH_2)_n(CONHONa)_2 + 4EtOH \xrightarrow{2HCl} (CH_2)_n(CONHOH)_2 + 2NaCl \quad (1)$$



$$(CH_2)_n(COCl)_2 + 2RNHOH + 2C_5H_5N \longrightarrow (CH_2)_n(CON(R)OH)_2 + 2C_5H_5N{\cdot}HCl \quad (2)$$

$$(R = C_6H_5,\ 2\text{-}CH_3C_6H_4,\ 4\text{-}CH_3C_6H_4,\ 4\text{-}ClC_6H_4)$$

given in Table III, showing the effect of variation of *n* on the nature of the spectra.

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Registry No. **1**, 7068-55-5; **2**, 38937-66-5; **3**, 20533-09-9; **4**, 89959-30-8; **5**, 89959-31-9; **6**, 89959-32-0; **7**, 28484-24-4; **8**, 89959-33-1; **9**, 89959-34-2; **10**, 89959-35-3; **11**, 20654-65-3; **12**, 89959-36-4; **13**, 89959-37-5; **14**, 89959-38-6; **15**, 89959-39-7; **16**, 89959-40-0; **17**, 89959-41-1; **18**, 89959-42-2; **19**, 89959-43-3; **20**, 89959-44-4; **21**, 89959-45-5; **22**, 89959-46-6; $(CH_2)_3(COOEt)_2$, 818-38-2; $(CH_2)_6(COOEt)_2$, 2050-23-9; $(CH_2)_2(COCl)_2$, 543-20-4; $(CH_2)_3(COCl)_2$, 2873-74-7; $(CH_2)_4(COCl)_2$, 111-50-2; $(CH_2)_6(COCl)_2$, 10027-07-3; $(CH_2)_8(COCl)_2$, 111-19-3; NH_2OH, 7803-49-8; C_6H_5NHOH, 100-65-2; 2-$CH_3C_6H_4NHOH$, 611-22-3; 4-$CH_3C_6H_4NHOH$, 623-10-9; 4-ClC_6H_4NHOH, 823-86-9.

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Thermal Stability of Nitrobenzyl Halogenides

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After a violent explosion occurred during the drying of *o*-nitrobenzyl bromide in a chemical factory, the thermal stability of nitrobenzyl halogenide isomers (X = Cl, Br) was studied by conventional thermoanalytical techniques (TGA, DSC) and by adiabatic calorimetry (ARC). All the nitrobenzyl halogenides tested decompose exothermally with abundant gas evolution. Bromide derivatives are less stable than chlorides; ortho isomers are less stable than meta and para isomers; *m*-nitrobenzyl bromide is slightly less stable than its para isomer, while *p*-nitrobenzyl chloride is slightly less stable than its meta isomer.

Introduction

Nitrobenzyl halogenides are an important group of intermediates for organic syntheses. Specific information on their thermal stability is almost nonexistent in the literature (*1*, *2*). Two papers refer to the possible explosive decomposition of *o*-nitrobenzyl bromide when heated above 125–130 °C (*3*, *4*). A violent explosion during the drying of this compound in a fine-chemicals factory (*5*) suggested that tests of the thermal stability be run on the nitrobenzyl halogenides (X = Cl, Br). The presence of NO_2 groups in organic molecules is generally an index of possible thermal instability. However, nitrobenzene is stable up to 300 °C (*6*).

To evaluate the influence of the substituents CH_2Cl and CH_2Br, and of their position on the thermal stability of nitrobenzene, the series of compounds listed in Table I was studied by conventional thermoanalytical techniques (TGA, DSC) and by adiabatic calorimetry (ARC).

Table I. Nitrobenzyl Halogenides Tested by Thermoanalytical Techniques and by Adiabatic Calorimetry

	purity, mol %
o-nitrobenzyl bromide	97
m-nitrobenzyl bromide	99
p-nitrobenzyl bromide	99
o-nitrobenzyl chloride	99
m-nitrobenzyl chloride	97
p-nitrobenzyl chloride	99

Experimental Section

Commercial-grade products (Aldrich, Beerse, Belgium) with purities between 97% and 99% were used without further treatment.

Instruments and Procedures. A Mettler TA 2000 C thermoanalyzer was used for the simultaneous recording on the same sample of TGA and DSC curves from room temperature to 1200 °C (*7*). An added module allows one to record the derivative of the TGA curve (DTG). Runs were performed at a heating rate of 10 °C min^{-1} on 5-mg samples, in air and in inert (nitrogen) atmosphere, with 40 mL min^{-1} gas flow. Platinum crucibles (0.15 mL) without caps were used.

A Mettler TA 3000 differential scanning calorimeter was used for testing in a sealed crucible (*8*). Runs were performed at a heating rate of 5 °C min^{-1} on 7–10-mg samples in Nimonic crucibles (0.5 mL), with gold safety disks resistant up to 10 000-kPa pressure.

In both experiments, aluminum oxide was used as an inert reference. The recorded temperature of the exotherm being an "instrumental temperature", depending mainly on the heating

Table II. DSC Tests in High-Pressure Crucibles (TA 3000)

	mp, °C	ΔH_{fus}, J g^{-1}	T_{decomp}, °C	T_{max}, °C	T_{fin}, °C	ΔH_{exo}, J g^{-1}	E_{att}, kJ mol^{-1}	ln K	n
o-nitrobenzyl bromide	46.6	63.9	112	175	210	1070	193.7	47.33	1.09
m-nitrobenzyl bromide	58.4	68.2	230 256	246 272	253 308	25 914			
p-nitrobenzyl bromide	102.2	105.7	230 258	245 273	250 300	22.5 806			
o-nitrobenzyl chloride	48.8	115	170	218	245	950	193	42.4	1.02
m-nitrobenzyl chloride	47.9	104	265	305	340	848			
p-nitrobenzyl chloride	70.3	121	244	284	320	832			

Table III. Isothermal Tests

	$T_{isothermal}$, °C	T_{decomp},[a] °C	T_{max}, °C	T_{fin}, °C	ΔH_{exo}, J g^{-1}	E_{act}, kJ mol^{-1}	ln K	n
o-nitrobenzyl bromide	80	110	175	220	1064	196.5	48.03	1.07
m-nitrobenzyl bromide	200[b]	195	241	290	591			
	180[c]	200	255	300	580			
	160	200	238	246	27			
		250	268	305	870			
p-nitrobenzyl bromide	200[d]	195	240	270	485			
	180	210	257	310	791			
o-nitrobenzyl chloride	160[e]	165	217	245	634	181.8	41.73	0.99
	140	165	217	245	937			
m-nitrobenzyl chloride	220	255	305	315	827			
p-nitrobenzyl chloride	200	235	278	310	838			

[a] Decomposition temperature after the "aging-cooling-heating" cycle. [b] After 15 min, exothermic peak (ΔH = 28 J g^{-1}). [c] After 75 min, exothermic peak (ΔH = 22 J g^{-1}). [a] After 20 min, exothermic peak (ΔH = 20 J g^{-1}). [e] After 60 min, weak exothermic peak.

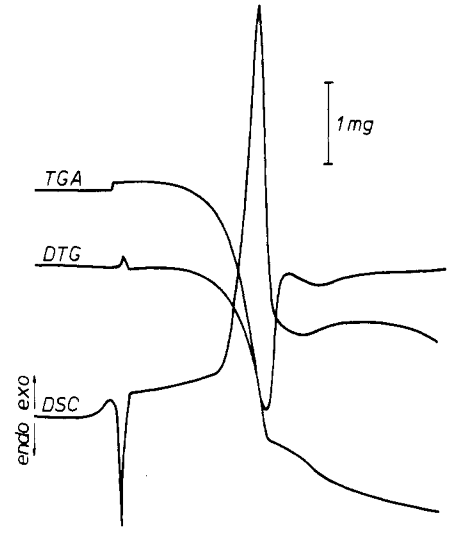

Figure 1. o-Nitrobenzyl bromide (5.31 mg) heated in an open crucible (TA 2000 C). Heating rate 10 °C min^{-1}; nitrogen (40 mL min^{-1}) atmosphere.

rate (*9*) the stability of the products was tested also at constant temperature (*10*). Samples were maintained in the TA 3000 for 2 h under isothermal conditions, at temperatures below decomposition as determined under dynamic conditions. After the run the samples were cooled to room temperature and reheated at 5 °C min^{-1}.

The accelerating rate calorimeter (ARC) used was from Columbia Scientific Industries (*5*, *11–15*). Spherical Hastelloy C bombs (20 g, 8 mL) were loaded with 0.8–1.0 g of product. Tests with o-nitrobenzyl bromide were performed also in a titanium bomb (9 g, 8 mL).

Results

Of the six compounds tested, only o-nitrobenzyl bromide reacts exothermally when heated in an open crucible (TA 2000 C) (Figure 1). The other five compounds, after melting, lose weight from 100 to 110 °C and are completely vaporized without decomposition. At 200–210 °C the weight loss is 100%.

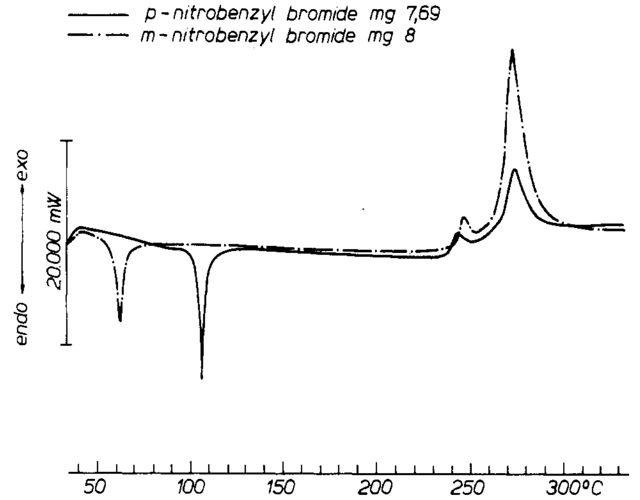

Figure 2. m- and p-nitrobenzyl bromide heated in a sealed crucible (TA 3000). Heating rate 5 °C min^{-1}.

In a sealed crucible (TA 3000) all the samples, after melting, decompose exothermally. The main exothermic peak of m- and p-nitrobenzyl bromide is preceded by a weak exotherm (Figure 2). Thermal and kinetic data from the "kinetic" program of the instrument (*16*) are reported in Table II. During isothermal heating m- and p-nitrobenzyl bromide and o-nitrobenzyl chloride undergo—after a certain time—a weak exothermic decomposition.

The samples, submitted to the "aging–cooling–heating" cycle, do not remelt, except p-nitrobenzyl bromide (temperature and ΔH of melting are lower than those of the unaged sample: 89.3 °C and 45 J g^{-1}). After the cycle, the starting temperature of the exotherm under dynamic conditions is—for all the compounds—lower than that of the unaged samples. Results are given in Table III.

The relevant data from the ARC tests, corrected to account for the Φ (*11*) factor are reported in Table IV.

Table IV. ARC Tests

	sample mass, g	degree of filling, g mL^{-1}	exptl data T_0, °C	T_{max}, °C	T_{fin}, °C	ΔT, °C	Φ[a]	calcd data ΔT, °C	T_{fin}, °C	ΔH, J g^{-1}
o-nitrobenzyl bromide	1.0	0.125	100	134	196	96	6.5	624	724	936
o-nitrobenzyl bromide[b]	0.96	0.120	100 170	142	170	70	5	350	450	504
m-nitrobenzyl bromide	0.893	0.112	176.54	213	255.85	79.31	7	555	731	832
p-nitrobenzyl bromide	0.930	0.116	186.50	216	261.11	74.61	6.9	515	701	772
o-nitrobenzyl chloride	0.933	0.116	144	196	230.11	86.11	6.9	594	738	891
m-nitrobenzyl chloride	0.839	0.104	213	245	284.06	71.06	7.5	533	746	800
p-nitrobenzyl chloride	0.877	0.109	202	240	275.01	73.01	7.3	533	735	800

[a] $\Phi = 1 + M_bC_b/MC$, where M_b, M, C_b, and C are the mass and the heat capacity of the Hastelloy C bombs (0.418 J (g °C)$^{-1}$ and of the sample (1.5 J (g °C)$^{-1}$). The high value of Φ results from the high reactivity of the compounds tested; for safety reasons, after a few preliminary runs, the sampling bombs were loaded with a relatively small amount of substance (0.8–1.0 g). [b] Titanium bomb.

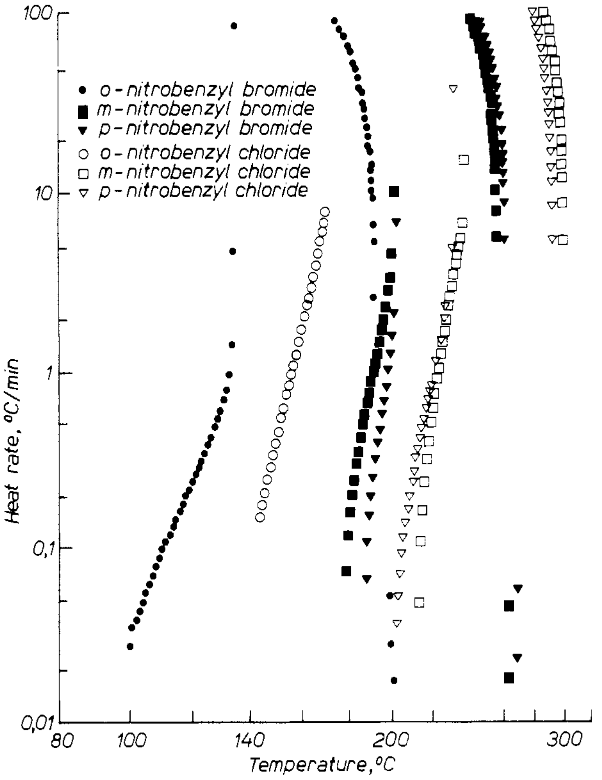

Figure 3. ARC data of heating rate vs. temperature in Hastelloy C bomb.

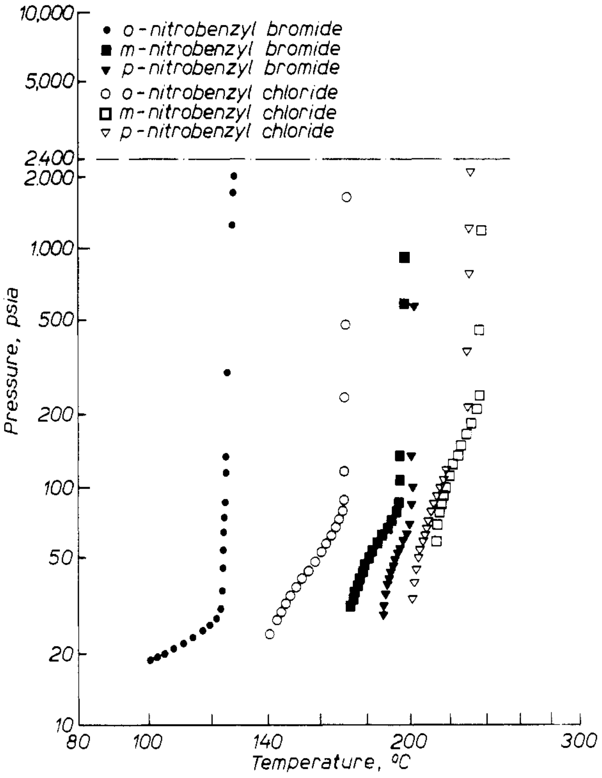

Figure 4. ARC data of pressure rise vs. temperature in Hastelloy C bomb. Safety valve setting 2400 psia.

Figure 3 reports the curve of heating rate vs. temperature for the six compounds. The curves show that the six compounds decompose through a rather complex mechanism. The shape of the initial branch of the curves (slope change after a few °C) is typical of an autocatalytic or radical reaction (*11*). At higher temperature, an inflection indicates a further change of mechanism. Above this temperature, the self-heating rate of all the samples increases to values so high (above 10 °C min^{-1}) that the instrument cannot maintain the adiabatic conditions and part of the reaction heat is transferred to the surroundings (*14*). During a few preliminary runs, when the heating rate reached such high values, the test was stopped by cooling the sample and circulating air into the calorimeter. In no case could the self-heating and pressure rise be arrested: decomposition always proceeded to completion. The curves of pressure rise vs. temperature, reported in Figure 4, show the violence of the decomposition. For all the samples, pressure exceeded 17 000 kPa (2500 psia); at this level the vent valve of the pressure-recording system intervened. Before the valve opened, in some cases pressure was increasing at a 2000 kPa min^{-1} rate.

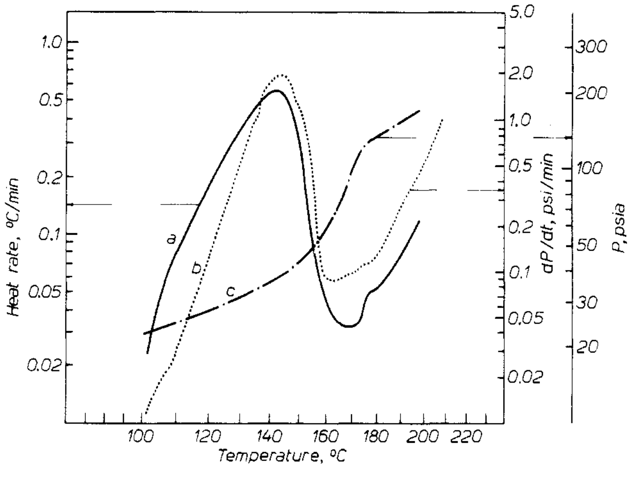

Figure 5. ARC data of *o*-nitrobenzyl bromide in titanium bomb: (a) heating rate vs. temperature; (b) pressure rise rate vs. temperature; (c) pressure rise vs. temperature.

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Figure 5 reports the self-heating rate and the pressure rise rate vs. temperature, as well as the pressure increase of *o*-nitrobenzyl bromide in a titanium bomb (*5*). The relevant data are reported in Table IV. Under adiabatic conditions the exothermicity of the first reaction is largely sufficient to raise the temperature above the starting temperature of the second reaction.

In the decomposition of *o*-nitrobenzyl bromide in a titanium bomb at least two exotherms take place. The titanium bomb, having a thermal inertia smaller than that of a Hastelloy C bomb, is more sensitive. Other runs on *o*-nitrobenzyl bromide with a higher degree of filling (0.15 g mL^{-1}) have shown, also in a titanium bomb, a behavior similar to that reported in Figure 3.

Discussion

The combined use of thermoanalytical techniques (TGA, DSC, ARC) under different experimental conditions—dynamic, isothermal, adiabatic (*17*)—has shown that all the nitrobenzyl halogenides tested decompose exothermally and violently, developing great amounts of gas. A scale of relative stability within this group of compounds can be based on the starting decomposition temperature from the DSC and ARC runs: (1) bromide derivatives are less stable than the corresponding chlorides; (2) ortho isomers are less stable than meta and para isomers; *m*-nitrobenzyl bromide is slightly less stable than *p*-nitrobenzyl bromide, while *p*-nitrobenzyl chloride is slightly less stable than *m*-nitrobenzyl chloride.

A regular correlation cannot be established of the stability of the isomers; this confirms the finding of other authors for the isomeric nitroanilines, nitrochlorobenzenes, nitrophenols, nitrotoluenes (*6*) and nitrobenzoyl chlorides (*18*).

ARC runs have recorded initial decomposition temperatures always lower than the DSC runs under dynamic conditions. This is justified by the higher sensitivity of the adiabatic calorimeter (0.4 W kg^{-1}) as related to the DSC (5 W kg^{-1}) (*17*) and by the fact that in the dynamic DSC runs the temperature of the thermal effect is a function of the heating rate (*9*).

The DSC 2-h isotherm runs after the ASTM (*10*) always gave starting decomposition temperatures very close to those from the ARC runs.

As for the decomposition mechanism, DSC runs under dynamic conditions show that *o*-nitrobenzyl bromide and chloride follow a first-order kinetics. The behavior of the other compounds apparently indicates a different, more complex kinetics. Further, *m*- and *p*-nitrobenzyl bromides decompose in two steps at least.

No kinetic information could be obtained from the ARC runs, due to the difficulty of maintaining the adiabaticity till the end of the decomposition process. Above a certain self-heating rate (10 °C min^{-1}) the system is not adiabatic; part of the reaction heat is transmitted to the surroundings. Therefore, the instrumental ΔT—and consequently the ΔH—from the ARC runs are surely smaller than those theoretically reached under strictly adiabatic conditions.

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Synthesis and Nuclear Magnetic Resonance Study of 2-Thiazolines

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A series of 5,5-dimethyl-2-thiazoline-4-carboxylates with a phenyl or methyl group at the 2-position of the ring were prepared from the corresponding methyl or ethyl ester of penicillamine and either methyl benzimidate or ethyl acetimidate. The free acid was obtained by the reaction of penicillamine with benzonitrile to produce 5,5-dimethyl-2-phenyl-2-thiazoline-4-carboxylic acid. Corresponding thiazolines were prepared from cysteine in the same manner. The nuclear magnetic resonance spectra of both series exhibit coupling of the methyl group at the 2-position with the hydrogen at the 4-position. The groups at the 5-position are nonequivalent and in the case of the cysteine series give rise to an ABX system. Further analysis confirms a concentration dependence for this splitting pattern.

Introduction

Recent studies (*1–6*) of copper complexes of the composition $[Cu^{II}_6Cu^{I}_8L_{12}Cl],^{Z\pm}$ where L = D-penicillamine, Z = 5– or L = 2,2-dimethylcysteamine, Z = 7+, have demonstrated the unique interactions of this class of chelate antidotes with copper. In the chronic form of copper intoxication known as Wilson's disease, the drug of choice has been the use of oral D-penicillamine. The intensely purple copper complexes of penicillamine and related ligands (*1–8*) have possible relevance to the treatment of Wilson's and other diseases (*9*, *10*). The stabilities of these very large mixed valence copper clusters appear to depend significantly on the structure of the ligand (*4*).

Attempts to prepare modified ligands from D-penicillamine (structure I, R_1 = Me, R_2 = H) require protection of the sulfur and nitrogen functional groups. A convenient direct method of

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