

# Organic Azides

# Organic Azides

## Syntheses and Applications

Editors

STEFAN BRÄSE

*Institute of Organic Chemistry,  
Karlsruhe Institute of Technology (KIT), Germany*

KLAUS BANERT

*Institute of Chemistry,  
Chemnitz University of Technology, Germany*

 **WILEY**

A John Wiley & Sons, Ltd., Publication

This edition first published 2010  
© 2010 John Wiley & Sons Ltd

*Registered office*

John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, United Kingdom

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at [www.wiley.com](http://www.wiley.com).

The right of the author to be identified as the author of this work has been asserted in accordance with the Copyright, Designs and Patents Act 1988.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the publisher.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book. This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is sold on the understanding that the publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The publisher and the author make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of fitness for a particular purpose. This work is sold with the understanding that the publisher is not engaged in rendering professional services. The advice and strategies contained herein may not be suitable for every situation. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of experimental reagents, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each chemical, piece of equipment, reagent, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the publisher nor the author shall be liable for any damages arising herefrom.

*Library of Congress Cataloging-in-Publication Data*

Organic azides : syntheses and applications / editors, Stefan Bräse, Klaus Banert.

p. cm.

Includes bibliographical references and index.

ISBN 978-0-470-51998-1 (cloth)

I. Azides. I. Bräse, Stefan II. Banert, Klaus.

QD305.N84O74 2009

547'.04—dc22

2009021624

A catalogue record for this book is available from the British Library.

ISBN 9780470519981

Set in 10 on 12 pt Times by Toppan Best-set Premedia Limited  
Printed and bound in Great Britain by CPI Antony Rowe Ltd, Chippenham, Wiltshire

# Contents

<i>Forewords: Rolf Huisgen, Valery Fokin, and Barry Sharpless</i>	xiii
<i>Preface</i>	xix
<i>List of Contributors</i>	xxi
<i>Abbreviations</i>	xxv
<b>PART 1: SYNTHESIS AND SAFETY</b>	<b>1</b>
<b>1 Lab-scale Synthesis of Azido Compounds: Safety Measures and Analysis</b>	<b>3</b>
<i>Thomas Keicher and Stefan Löbbecke</i>	
1.1 Introduction	3
1.2 Properties that Impose Restrictions on Lab-scale Handling of Azides	4
1.2.1 Hydrazoic Acid and Its Metal Salts	4
1.2.2 Organic Azides	5
1.3 Laboratory Safety Instructions for the Small-scale Synthesis of Azido Compounds	5
1.4 Analyzing Safety-related Properties of Azides	7
1.4.1 Impact Sensitivity Testing	7
1.4.2 Friction Sensitivity Testing	9
1.4.3 ESD Testing	11
1.4.4 Thermoanalytical Measurements	13
1.4.5 Calorimetric and Gravimetric Stability Tests	19
1.4.6 Koenen Test	23
References	25
<b>2 Large-scale Preparation and Usage of Azides</b>	<b>29</b>
<i>Jürgen Haase</i>	
2.1 Introduction	29
2.2 Precursor Azides, Technical Production and Properties	30
2.2.1 Sodium azide (NaN <sub>3</sub> )	30
2.2.2 Trimethylsilyl Azide (TMSA)	31
2.2.3 Diphenylphosphoryl Azide (DPPA)	32
2.2.4 Tributyltin Azide (TBSnA)	34
2.2.5 Azidoacetic Acid Ethyl Ester (AAE)	35

2.2.6	Tetrabutylammonium Azide (TBAA)	35
2.2.7	Others	37
2.3	Examples for the Use of Azides on a Technical Scale	37
2.3.1	Addition of $\text{NaN}_3$ to Multiple CC- or CN-Bonds	37
2.3.2	Addition of $\text{Alk-N}_3$ and $\text{Ar-N}_3$ to Multiple CC- and/or CN-Bonds	43
2.3.3	Carboxylic Acid Azides: Precursors for Isocyanates	43
2.3.4	Organic Azides: Ring Opening Reaction on Oxiranes and Aziridines: Paclitaxel, Tamiflu <sup>®</sup>	43
2.3.5	Organic Azides: Protective Group, Masked Amines	45
2.3.6	Organic Azides: Cross-linking Agents for Polymers	47
2.4	The Future of Commercial-scale Azide Chemistry	47
	References	48
<b>3</b>	<b>Synthesis of Azides</b>	<b>53</b>
	<i>Teresa M.V.D. Pinho e Melo</i>	
3.1	Introduction	53
3.2	Synthesis of Alkyl Azides	53
3.2.1	Classic Nucleophilic Substitutions: Azides from Halides, Sulfonates, Sulfites, Carbonates, Thiocarbonates and Sulfonium Salts	53
3.2.2	Azides by Ring Opening of Epoxides and Aziridines	64
3.2.3	Azides by the Mitsunobu Reaction	70
3.2.4	Alkyl Azides from Amines	71
3.2.5	Alkyl Azides from Carbon Nucleophiles and Electron-poor Sulfonyl Azides	75
3.3	Synthesis of Aryl Azides	76
3.3.1	Nucleophilic Aromatic Substitution: $\text{S}_{\text{N}}\text{Ar}$ Reactions	76
3.3.2	Aryl Azides from Diazonium Compounds	80
3.3.3	Aryl Azides from Organometallic Reagents	80
3.3.4	Aryl Azides by Diazo Transfer	83
3.3.5	Aryl Azides from Hydrazines and from Nitrosoarenes	84
3.4	Synthesis of Acyl Azides	84
3.4.1	Acyl Azides from Mixed Acid Chlorides	84
3.4.2	Acyl Azides from Mixed Anhydrides	85
3.4.3	Acyl Azides by Direct Conversion of Carboxylic Acids	86
3.4.4	Acyl azides by Direct Conversion of Aldehydes	88
3.4.5	Acyl Azides by Direct Conversion of Acylhydrazines	89
3.4.6	Acyl Azides from N-acylbenzotriazoles	89
	References	90
<b>4</b>	<b>Azides by Olefin Hydroazidation Reactions</b>	<b>95</b>
	<i>Jérôme Waser and Erick M. Carreira</i>	
4.1	Introduction	95
4.2	Conjugate Addition of Hydrazoic Acid and Its Derivatives	96

4.3	Addition of Hydrazoic Acid and Its Derivatives to Non-Activated Olefins	98
4.4	Cobalt-Catalyzed Hydroazidation	99
4.4.1	Optimization of the Cobalt-Catalyzed Hydroazidation Reaction	99
4.4.2	Scope of the Hydroazidation of Olefins	101
4.4.3	Further Process Optimization	102
4.4.4	One-pot Functionalization of the Azide Products	106
4.4.5	Mechanistic Investigations	108
4.5	Conclusion	109
	References	109
<b>PART 2: REACTIONS</b>		<b>113</b>
<b>5</b>	<b>The Chemistry of Vinyl, Allenyl, and Ethynyl Azides</b>	<b>115</b>
	<i>Klaus Banert</i>	
5.1	Introduction and Early Synthetic Methods for Vinyl Azides	115
5.2	Routes to Vinyl Azides Developed in the Period 1965–70	119
5.3	New Methods to Prepare Vinyl Azides	126
5.4	Reactions of Vinyl Azides	133
5.5	The Chemistry of Allenyl Azides	147
5.6	Generation of Ethynyl Azides	154
5.7	Conclusion	156
	Acknowledgment	157
	References	157
<b>6</b>	<b>Small Rings by Azide Chemistry</b>	<b>167</b>
	<i>Thomas L. Gilchrist and Maria José Alves</i>	
6.1	Introduction	167
6.2	2 <i>H</i> -Azirines	167
6.3	Aziridines	171
6.3.1	Aziridines <i>via</i> Nitrene Intermediates	172
6.3.2	Aziridines <i>via</i> Triazolines	176
6.3.3	Aziridines from Epoxides or 1,2-Diols	181
6.3.4	Aziridines from Vinyl Azides <i>via</i> 2 <i>H</i> -Azirines	183
6.4	Triaziridines	185
6.5	Azetidinones	186
	References	187
<b>7</b>	<b>Schmidt Rearrangement Reactions with Alkyl Azides</b>	<b>191</b>
	<i>Scott Grecian and Jeffrey Aubé</i>	
7.1	Introduction and Early Attempts (1940–60)	191
7.2	Schmidt Reactions of Alkyl Azides with Carbonyl Compounds	193
7.2.1	Intramolecular Reactions	193
7.2.2	Intermolecular Reactions	197
7.2.3	Reactions of Hydroxyalkyl Azides	200

7.3	Schmidt Reactions of Alkyl Azides with Carbocations	207
7.4	Metal-mediated Schmidt Reactions of Alkyl Azides with Alkenes and Alkynes	211
7.5	Reactions of Alkyl Azides with $\alpha,\beta$ -Unsaturated Ketones	214
7.6	Reactions of Alkyl Azides with Epoxides	216
7.7	Combined Schmidt Rearrangement Cascade Reactions	218
7.8	Schmidt Rearrangements in the Total Synthesis of Natural Products	221
7.9	Schmidt Rearrangements of Alkyl Azides in the Synthesis of Interesting Non-natural Products	229
7.10	Schmidt Rearrangements of Hydroxyalkyl Azides toward Biologically Relevant Compounds	232
7.11	Final Comments	234
	Acknowledgments	235
	References	235
<b>8</b>	<b>Radical Chemistry with Azides</b>	<b>239</b>
	<i>Ciril Jimeno and Philippe Renaud</i>	
8.1	Introduction	239
8.2	Addition of the Azidyl Radical onto Alkenes	241
8.2.1	Metal Generated Azidyl Radicals	241
8.2.2	Azidation Using Hypervalent Iodine Compounds	243
8.2.3	Halogen Azides as a Source of Azidyl Radicals	244
8.2.4	Electrochemically Generated Azidyl Radicals	246
8.3	Azidation of Carbon Centered Radicals	246
8.3.1	Radical Azidation	247
8.3.2	Radical Additions to Alkyl and Aryl Azides	255
8.4	Aminyl and Amidyl Radicals <i>via</i> Reduction of Azides	255
8.4.1	Photo- and Electrochemical Reductions of Organic Azides to Amines	257
8.4.2	Reduction of Organic Azides with Metals	257
8.4.3	Reduction of Organic Azides with $\text{SmI}_2$	258
8.4.4	Radical Reactions of Organic Azides with Tributyltin Hydride	259
8.4.5	Radical Reductions of Organic Azides with Silanes	260
8.4.6	Radical Reactions of Organic Azides with $\text{FeCl}_2$	261
8.5	Fragmentation Reaction of $\alpha$ -Azidoalkyl Radicals	262
8.6	Conclusions	264
	References	264
<b>9</b>	<b>Cycloaddition Reactions with Azides: An Overview</b>	<b>269</b>
	<i>Christine Schilling, Nicole Jung and Stefan Bräse</i>	
9.1	Huisgen 1,3-dipolar cycloaddition	269
9.2	Copper-Catalyzed Azide-Alkyne Cycloaddition (CuAAC)	270
9.2.1	General Aspects of the CuAAC Reaction	270
9.2.2	Mechanism of the CuAAC Reaction	271

9.3	Acceleration of the Click Reaction	272
9.3.1	Addition of Ligands	272
9.3.2	Addition of Base	273
9.4	Copper-free Click Chemistry	274
9.5	Ruthenium-Catalyzed Azide-Alkyne Cycloaddition (RuAAC)	275
9.6	Use of Other Metals for the Cycloaddition of Azides and Alkynes: Ni(II), Pt(II), Pd(II)	277
9.7	Cycloaddition Reactions with Azides for the Synthesis of Tetrazoles	278
9.7.1	Intermolecular Approaches	278
9.7.2	Intermolecular Approaches	280
9.8	Click Chemistry for the Synthesis of Dihydrotriazoles	280
9.9	Cycloaddition Reactions with Azides to Give Thiatriazoles	282
	References	282
<b>10</b>	<b>Dipolar Cycloaddition Reactions in Peptide Chemistry</b>	<b>285</b>
	<i>Christian Wenzel Tornøe and Morten Meldal</i>	
10.1	Introduction	285
10.2	Amino Acid Derivatives by DCR	286
10.3	Peptide Backbone Modifications by DCR	288
10.4	Other Peptide Modifications by DCR	292
10.5	Macrocyclization by DCR	302
10.6	Dendrimers and Polymers	305
10.7	Isotopic Labeling by DCR	307
10.8	Perspective	308
	References	309
<b>11</b>	<b>Photochemistry of Azides: The Azide/Nitrene Interface</b>	<b>311</b>
	<i>Nina Gritsan and Matthew Platz</i>	
11.1	Introduction	311
11.2	Photochemistry of Hydrazoic Acid (HN <sub>3</sub> )	312
11.3	Photochemistry of Alkyl Azides	315
11.4	Photochemistry of Vinyl Azides	319
11.5	Photochemistry of Carbonyl Azides and Azide Esters	321
11.5.1	Photochemistry of Azide Esters	325
11.6	Photochemistry of Phenyl Azide and Its Simple Derivatives	327
11.6.1	Photochemistry of Phenyl Azide	327
11.6.2	Photochemistry of Simple Derivatives of Phenyl Azide	336
11.6.3	Photochemistry of Polynuclear Aromatic Azides	355
11.7	Conclusion	363
	Acknowledgments	364
	References	364
<b>12</b>	<b>Organoazides and Transition Metals</b>	<b>373</b>
	<i>Werner R. Thiel</i>	
12.1	Introduction	373
12.2	Metal Complexes Co-crystallized with an Organoazide	376

12.3	Cationic Metal Complexes with Organoazide Containing Anions	376
12.4	Metal Complexes with Ligands Bearing a Non-coordinating Organoazide Unit	377
12.5	Metal Complexes with an Intact, Coordinating and Linear Organoazide Ligand	383
12.6	Metal Complexes with an Intact, Coordinating but Bent Organoazide Ligand	384
12.7	Organoazides Reacting with Other Metal Bound Ligands	385
	References	387
<b>PART 3: MATERIAL SCIENCES</b>		<b>389</b>
<b>13</b>	<b>Azide-containing High Energy Materials</b>	<b>391</b>
	<i>Thomas M. Klapötke and Burkhard Krumm</i>	
13.1	Introduction	391
13.2	Organic Azides	391
13.2.1	Alkyl and Alkenyl Substituted Azides	392
13.2.2	Aryl Substituted Azides	400
13.2.3	Heterocycles Containing Azide Groups	405
	Acknowledgments	409
	References	409
<b>14</b>	<b>Azide Chemistry in Rotaxane and Catenane Synthesis</b>	<b>413</b>
	<i>Stéphanie Durot, Julien Frey, Jean-Pierre Sauvage and Christian Tock</i>	
14.1	Introduction	413
14.2	Purely Organic Rotaxanes and Catenanes	415
14.2.1	With Cucurbiturils (CB) and Cyclodextrins (CD) as Cyclic Components	415
14.2.2	Based on Hydrogen Bonding or on Organic Donor-Acceptor Complexes	417
14.3	Transition Metal Templated Approaches	424
14.3.1	Cu(I) Assembled Rotaxanes	424
14.3.2	Cu(I) as Both a Template and a Catalyst	428
14.4	Conclusion	432
	References	433
<b>PART 4: APPLICATION IN BIOORGANIC CHEMISTRY</b>		<b>437</b>
<b>15</b>	<b>Aza-Wittig Reaction in Natural Product Syntheses</b>	<b>439</b>
	<i>Francisco Palacios, Concepción Alonso, Domitila Aparicio, Gloria Rubiales and Jesús M. de los Santos</i>	
15.1	Introduction	439
15.2	Intermolecular Aza-Wittig Reaction	440
15.2.1	Reaction with Carbonyl Compounds	440
15.2.2	Reaction with Heterocumulene Derivatives	446

15.3	Intramolecular Aza-Wittig Reaction	451
15.3.1	Functionalized Phosphazenes Containing an Aldehyde Group	451
15.3.2	Functionalized Phosphazenes Containing a Ketone Group	454
15.3.3	Functionalized Phosphazenes Containing an Ester Group	459
15.3.4	Functionalized Phosphazenes Containing an Amide Group	461
15.4	Conclusions	464
	Acknowledgments	465
	References	466
<b>16</b>	<b>Azides in Carbohydrate Chemistry</b>	<b>469</b>
	<i>Henning S.G. Beckmann and Valentin Wittmann</i>	
16.1	Introduction	469
16.2	Synthesis of Azide-Containing Carbohydrates	470
16.3	Azides as Protecting Groups during Aminoglycoside Synthesis	472
16.4	Azides as Non-Participating Neighboring Groups in Glycosylations	474
16.5	Glycosyl Azides as Precursors for Glycosyl Amides	475
16.6	Synthesis of Glycoconjugates <i>via</i> Azide-Alkyne [3+2] Cycloaddition	478
16.7	Metabolic Oligosaccharide Engineering	483
	References	486
	<b><i>Index</i></b>	<b>491</b>

# Foreword

Whenever the significance of a chemical discovery is ubiquitously recognized, a swarm of research groups will quickly join (and compete) in developing the ‘new territory’. Take the finding of [60]fullerene as a new modification of elemental carbon: the evolution of a new research area boomed, an exponential growth in the number of publications being the consequence.

In the early history of organic chemistry, new discoveries – there were so many! – struck less of an echo; there were so few chemists. Peter Griess, a German chemist in a British brewery, prepared the first aromatic diazonium salts (1858) and, on his own, unveiled their rich reactivity, the azo coupling with phenolates included. The reaction of arenediazonium perbromides with ammonia provided aryl azides (1864).<sup>1</sup> After Griess’ death (1888), three obituaries by August Wilhelm von Hofmann, Emil Fischer, and Heinrich Caro praised the ‘single combatant’.<sup>2-4</sup>

The azide story vigorously unfolded when Theodor Curtius, the grandseigneur of nitrogen chemistry, entered the scene. The preparation of ethyl diazoacetate, the first aliphatic diazo compound (1883),<sup>5</sup> paved the way to hydrazine *via* ‘bisdiazoacetate’ (1887).<sup>6</sup> Several steps in Curtius’ career – moves from Munich to Erlangen and further to Kiel (later to Bonn and Heidelberg) – hardly curbed the momentum of basic discoveries. The reaction of benzoyl hydrazine with nitrous acid provided benzoyl azide, and alkaline hydrolysis gave sodium azide. By acidification of the latter, ‘azoimid’  $\text{HN}_3$  was set free (1890),<sup>7</sup> a gas of ‘highly peculiar, dreadfully pungent smell’. The preparation of alkyl azides from  $\text{AgN}_3$  and alkyl iodides was likewise found in Curtius’ laboratory.

In hot ethanol, benzoyl azide was converted to ethyl *N*-phenylcarbamate (1894). This ‘Curtius rearrangement’ was recognized by its discoverer as a general method of degrading carboxylic acids to amines,<sup>8</sup> whereas the intermediacy of isocyanates escaped him.

There was no overlooking the explosive character of azides. Curtius described a sample of aqueous hydrogen azide on local heating giving rise to a ‘formidable detonation and disintegration of the thick-walled glass tube to dust’. And furthermore: ‘The detonation which a few mg of silver azide generate on impact or heating is unparalleled.’ In World War I lead azide replaced the mercury fulminate as initiator.

Thus, azides gained the bad reputation of being dangerous in handling rather early (see Chapter 13). Explosives are ‘energy-rich’ or ‘high-energy’ compounds in technical jargon, since they serve as a source of energy. More correctly, there is an increase of bond energy due to the formation of  $\text{N}_2$  in the explosion, and the pressure of the produced gases contributes to the destructive force. A rule of thumb in the preparative use of organic azides:

the explosion danger decreases with diminishing fraction of  $N_3$  in the molecular mass; e.g., phenyl azide is easier to handle than methyl azide.

Whereas P. Griess abstained from drafting a structure for the  $N_3$  unit, Th. Curtius and contemporaries formulated azides as cyclic 1*H*-triazirines. A. Angeli<sup>9</sup> and J. Thiele<sup>10</sup> found an open-chain azide group more consistent with the reactivity spectrum; still, the open formula bore the blemish of a pentavalent middle nitrogen. This flaw was overcome by the resonance description of  $R-N_3 : N_\beta$  appears as iminium function, whereas  $N_\alpha$  and  $N_\gamma$  share the anionic charge (Sutton, 1931).<sup>11</sup> X-ray analyses and many physical methods confirmed this open-chain formula of azides. In modern terminology, by the way, 1*H*-triazirines constitute antiaromatic  $4\pi$  systems.

Curtius dreamed of  $HN_5$  and derivatives, the more so as pentazole was the ‘missing link’ in the azole series. The reaction of benzenediazonium chloride and sodium azide furnished phenyl azide and  $N_2$  instead of the desired phenylpentazole (Arthur Hantzsch, 1903).<sup>12</sup> In fact, part of the reaction passes through phenylpentazole, as unambiguously shown by a combination of kinetics and  $^{15}N$ -labeling (Clusius, Huisgen, & Ugi, 1956).<sup>13</sup> Some arylpentazoles were obtained crystalline, but extrude  $N_2$  in solution to give aryl azides. What about the parent  $HN_5$ ? In a study of 2008, Richard Butler *et al.* oxidatively dearylated *p*-anisylpentazoles, which differed in the position of the  $^{15}N$ -label, and the  $^{15}N$ -distribution in  $N_3^-$ , appears to be in harmony with the fleeting occurrence of  $HN_5/N_5^-$ .<sup>14</sup>

There is no place for pentazole in Beilstein’s *Handbook of Organic Chemistry*. What is the organic compound with the highest nitrogen content? Tetraazidomethane with 93% N merits this reputation; the recently prepared  $CN_{12}$  is a highly explosive liquid (Banert, 2007).<sup>15</sup>

The application of azides as carboxy-activating group in peptide synthesis goes back to Curtius, too. On treating *N*-benzoylglycyl azide with glycine in aqueous alkali, *N*-benzoylglycylglycine was obtained. Renewed conversion to the azide allowed a repetitive procedure by which the *N*-benzoyltetrapeptide was achieved (1902).<sup>16</sup> The actual significance of the azide method is based on avoiding the feared racemization.

In 1893, Arthur Michael observed the formation of a 1,2,3-triazole derivative in the reaction of ‘diazobenzolimid’ (i.e.  $Ph-N_3$ ) with dimethyl acetylenedicarboxylate;<sup>17</sup> Michael – a future Harvard professor – worked with R. Bunsen and A.W. von Hofmann. Numerous cycloadditions of organic azides and  $HN_3$  to alkynes and alkenes were described in the sequel. In the general definition and classification azides belong to the 1,3-dipoles of propargyl-allenyl type (R. Huisgen, 1960).<sup>18</sup> 1,3-Dipolar cycloadditions share the  $6\pi$ -electron balance with Diels-Alder reactions – and the wide synthetic application. Albert Padwa edited monographs on 1,3-dipolar cycloaddition chemistry in 1984 and 2003 – substantial chapters on azides were included.<sup>19</sup>

Rate constants ( $k_2$ ) for cycloadditions of phenyl azide to substituted ethylenes and acetylenes stretch over seven magnitudes; high values were observed for enamines, moderate  $k_2$  for the acrylic ester type, and the rate minimum was found for common alkenes and alkynes (Huisgen, Szeimies, & Möbius, 1967).<sup>20</sup> In the PMO treatment of concerted cycloadditions, Reiner Sustmann found the key to the understanding of substituent effects; e.g., a plot of  $k_2$  for the cycloadditions of  $Ph-N_3$  versus the ionization potential of substituted ethylenes and acetylenes furnished a degenerate U shape (1971).<sup>21</sup> Such a plot is a distinguishing feature for each 1,3-dipole and reflects the specific mix of nucleophilic and electrophilic activity, modified by steric effects.

The 1,3-cycloaddition of alkyl azides to terminal alkynes is very slow, but can be catalyzed by Cu(I) (mechanism: Straub, 2007).<sup>22</sup> This formation of 1,2,3-triazoles, popularized as ‘click reaction’, was used by Sharpless and Meldal (both 2002)<sup>23,24</sup> for the selective and biocompatible ligation of peptides, proteins, and especially for the introduction of biomarkers. *In vivo* applications in aqueous medium are feasible. The bioresearch community applauded this new tool which aroused fresh enthusiasm in azide chemistry.

In preparative and synthetic application, organic azides unfold an astonishing versatility and witnessed a renaissance in recent decades; a renaissance to which the two editors successfully contributed. A recent review is entitled ‘An Exploding Diversity of a Unique Class of Compounds’ (Bräse, 2005),<sup>25</sup> and a yearly increase by more than a thousand publications on organic azides is mentioned. This profusion is intimidating and demonstrates the necessity of a multi-authored monograph. The editors succeeded in dividing the abundance in handy packages and in persuading competent experts to write the chapters. A certain overlap among the chapters is not harmful, is even desirable, since not every user will devour the whole book. The monograph offers access to the most recent state of research. The faster such a monograph may become obsolete, the higher has been its benefit to the chemical community.

Rolf Huisgen  
LMU München

## References

- [1] P. Griess, *Proc. R. Soc. London* **1864**, 13, 375–84. P. Griess, *Liebigs Ann. Chem.* **1866**, 137, 39–91.
- [2] A.W. von Hofmann, *Ber. Dtsch. Chem. Ges.* **1891**, 24, 1007–57.
- [3] E. Fischer, *Ber. Dtsch. Chem. Ges.* **1891**, 24, 1058–78.
- [4] H. Caro, *Ber. Dtsch. Chem. Ges.* **1891**, 24, I–XXXVIII.
- [5] Th. Curtius, *Ber. Dtsch. Chem. Ges.* **1883**, 16, 2230–1.
- [6] Th. Curtius, *Ber. Dtsch. Chem. Ges.* **1887**, 20, 1632–4.
- [7] Th. Curtius, *Ber. Dtsch. Chem. Ges.* **1890**, 23, 3023–33.
- [8] Th. Curtius, *Ber. Dtsch. Chem. Ges.* **1894**, 27, 778–81; Th. Curtius, *J. Prakt. Chem.* **1894**, 50, 275–94.
- [9] A. Angeli, *Atti Reale Accad. Lincei* **1907**, 16 II, 790.
- [10] J. Thiele, *Ber. Dtsch. Chem. Ges.* **1911**, 44, 2522–4.
- [11] L.E. Sutton, *Nature* **1931**, 128, 639. N.V. Sidgwick, L.E. Sutton, W. Thomas, *J. Chem. Soc.* **1933**, 406–12.
- [12] A. Hantzsch, *Ber. Dtsch. Chem. Ges.* **1903**, 36, 2056–8.
- [13] R. Huisgen, I. Ugi, *Angew. Chem.* **1956**, 68, 705–6. I. Ugi, R. Huisgen, K. Clusius, M. Vecchi, *Angew. Chem.* **1958**, 68, 753–4.
- [14] R.N. Butler, J.M. Hanniffy, J.C. Stephens, L.A. Burke, *J. Org. Chem.* **2008**, 73, 1354–64.
- [15] K. Banert, Y.H. Joo, T. Ruffer, B. Walfort, H. Lang, *Angew. Chem.* **2007**, 119, 1187–90; *Angew. Chem. Int. Ed.* **2007**, 46, 1168–71.
- [16] Th. Curtius, *Ber. Dtsch. Chem. Ges.* **1902**, 35, 3326–8. Th. Curtius, A. Benrath, *Ber. Dtsch. Chem. Ges.* **1904**, 37, 1279–84.
- [17] A. Michael, *J. Prakt. Chem.* **1893**, 48, 94–5.
- [18] R. Huisgen, Centenary Lecture 1960; *Proc. Chem. Soc.* **1961**, 357–69. R. Huisgen, *Angew. Chem.* **1963**, 75, 604–37; *Angew. Chem. Int. Ed.* **1963**, 2, 565–98.

- [19] A. Padwa (ed.), *1,3-Dipolar Cycloaddition Chemistry*, John Wiley & Sons, Inc., New York, **1984**. A. Padwa, W.H. Pearson (eds.), *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Towards Heterocycles and Natural Products*, John Wiley & Sons, Inc., New York, **2003**.
- [20] R. Huisgen, G. Szeimies, L. Möbius, *Chem. Ber.* **1967**, *100*, 2494–2507.
- [21] R. Sustmann, H. Trill, *Angew. Chem.* **1972**, *84*, 887–8; *Angew. Chem. Int. Ed.* **1972**, *11*, 838–9. R. Sustmann, *Pure Appl. Chem.* **1974**, *40*, 569–93.
- [22] C. Nolte, P. Mayer, B.F. Straub, *Angew. Chem.* **2007**, *119*, 2147–9; *Angew. Chem. Int. Ed.* **2007**, *46*, 2101–3. B.F. Straub, *Chem. Commun.* **2007**, 3868–70.
- [23] V.V. Rostovtsev, L.G. Green, V.V. Fokin, K.B. Sharpless, *Angew. Chem.* **2002**, *114*, 2708–11; *Angew. Chem. Int. Ed.* **2002**, *41*, 2596–9.
- [24] C.W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057–64.
- [25] S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem.* **2005**, *117*, 5320–74; *Angew. Chem. Int. Ed.* **2005**, *44*, 5188–240.

# Foreword

It is a privilege to write a few words here about our favorite functional group – organic azides. Both of us were fortunate to read (in truth memorize) the two-volume monograph ‘Chemistry of Open-Chain Organic Nitrogen Compounds’ by P.A.S. Smith; K.B.S. in 1966, its year of publication, and V.V.F almost four decades later. Despite this time gap, Smith’s great style and deep knowledge – both physical and descriptive, made for a fantastic story for both of us, start to finish. We are convinced it is still the only guaranteed way to get injected with ‘the right stuff’ – assuming it’s mastery of nitrogen reactivity you seek!

What Smith had liked, and thence taught best about nitrogen, was that it was the only element in the first row which engaged in fast and loose atom transfer redox events, thanks to the panoply of fast reactions open to its oxidation states III and lower. In other words, nitrogen species could be slippery and redox-able like the transition metals we know so well.

Among reactive organic groups, azides are near the top energetically, and yet paradoxically they are *kinetically* locked up. Nevertheless, the fear of the energy these small energetic groups pack, the sort of ‘azidophobia’, has curtailed the ideas and experiments needing organic azides. Although they have been known for over 100 years, the utility of organic azides has been often limited to the facile introduction of the amino group into organic molecules. Other facets of their razor-sharp reactivity remained largely unexplored until relatively recent years. Yet organic azides are versatile sources of nitrenes, amines, and nitrogen heterocycles containing three contiguous nitrogen atoms. The latter are a foreign territory for nature and hence, unique tools for studying it.

Bertozzi recognized nearly bioorthogonal properties of azides and the ease of their introduction into the biological molecules, and pioneered their reaction with phosphines in her studies of biological processes. Around the same time, Finn and Sharpless ‘saw’ that Rolf Huisgen’s 1,3-dipolar cycloadditions of azides and alkynes forming triazoles was *the cream of the crop* among all known organic transformations. The alkyne and the azide groups are nearly completely *orthogonal* to all terrestrial environments – including *inter alia*, the fluids and tissues of live organisms. They either react with each other or not at all, so are in effect invisible, which endows them for stealth-like uses, such as discovery of enzyme inhibitors through target guided ‘*in situ* click chemistry.’

Shortly thereafter, Fokin’s discovery of the reactivity of in situ-generated copper acetylides with azides in aqueous solutions made the copper-catalyzed azide-alkyne

cycloaddition (CuAAC) one of the most widely utilized reactions involving organic azides.

We are often asked if there are more ‘orthogonal’ click reactions like the CuAAC and the thiol-ene addition lurking out there. The answer is a confident ‘yes’. However, when people want to replace the azide group with another 1,3-dipole, this is hard to imagine, assuming one demands identical, or better reactivity parameters. The simple reason is that the other dipoles are not adequately ‘invisible’ in the acid-base world. Hence, the azide functionality should remain a rich source of new reactivity discoveries for many years.

From our own experience, and wisdom gleaned from the likes of Peter Smith, Thomas Archibald, and Alfred Hassner, we say get ready for the arrival of more azides in applied chemistry. They may be late bloomers, but they’re coming on strong. In fact, the best evidence for the ascendancy of organic azides in synthesis is right here, in this outstanding collection of reviews on the topic edited by Stefan Bräse and Klaus Banert.

*K. Barry Sharpless and Valery V. Fokin  
La Jolla, California*

# Preface

This book is aimed at graduate students or researchers, who have basic knowledge in organic chemistry and want to approach the field of organic azides from a historical perspective through to the state-of-the-art. The material will be suitable for supplementing a graduate course in organic syntheses.

The contributing authors are leading scientists in their field. Each individual was asked to contribute 20–30 printed pages putting their own research in the context of the development of the chemistry of organic azides. This material has been organized into 16 chapters.

# List of Contributors

**Concepción Alonso**, Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco. Apartado 450. 01080 Vitoria, Spain

**Maria José Alves**, Departamento de Química, Campus Gualtar, Universidade do Minho, P-4710057 Braga, Portugal

**Domitila Aparicio**, Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco. Apartado 450. 01080 Vitoria, Spain

**Jeffrey Aubé**, Department of Medicinal Chemistry, University of Kansas, School of Pharmacy, Malott Hall, 1251 Wescoe Hall Drive, Room 4070, Lawrence, KS 66045-7582, USA

**Klaus Banert**, Institute of Chemistry, Chemnitz University of Technology, Strasse der Nationen 62, 09111 Chemnitz, Germany

**Henning S.G. Beckmann**, Fachbereich Chemie, Universität Konstanz, Universitätsstr. 10, D-78457 Konstanz, Germany

**Stefan Bräse**, Institute of Organic Chemistry, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6, Karlsruhe, D-76131, Germany

**Erick M. Carreira**, Laboratorium für Organische Chemie, HCI H 335, Wolfgang-Pauli-Str. 10, 8093 Zürich, Switzerland

**Stéphanie Durot**, Institut de Chimie, CNRS et Université de Strasbourg, UMR 7177 Laboratoire de Chimie-Organico-Minérale, 4 rue Blaise Pascal, BP 1032, F-67070 Strasbourg cedex, France

**Julien Frey**, CEA Saclay, iBiTec-S, Service de Bioénergétique, Biologie Structurale et Mécanismes. 91191 Gif-sur-Yvette, France

**Thomas L. Gilchrist**, Cunningham Drive, Wirral, CH63 0JX, UK

**Scott Grecian**, Lacamas Laboratories, 3625 North Suttle Road, Portland, Oregon 97217, USA

**Nina Gritsan**, Institute of Chemical Kinetics and Combustion of Siberian Branch of Russian Academy of Sciences, Novosibirsk, Russia

**Jürgen Haase**, Dynamit Nobel GmbH, Explosivstoff und Systemtechnik, Kalkstrasse 218, 51377 Leverkusen, Germany

**Ciril Jimeno**, University of Bern, Department of Chemistry and Biochemistry, Freiestrasse 3, CH-3012 Bern, Switzerland

**Nicole Jung**, Institute of Organic Chemistry, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6, Karlsruhe, D-76131, Germany

**Thomas Keicher**, Fraunhofer Institut für Chemische Technologie ICT, Pfinztal, Germany

**Thomas M. Klapötke**, Department Chemie und Biochemie, Ludwig-Maximilians-Universität München, Butenandtstr. 5-13(D), D-81377 Munich, Germany

**Burkhard Krumm**, Department Chemie und Biochemie, Ludwig-Maximilians-Universität München, Butenandtstr. 5-13(D), D-81377 Munich, Germany

**Stefan Löbbecke**, Fraunhofer Institut für Chemische Technologie ICT, Pfinztal, Germany

**Morten Meldal**, Carlsberg Laboratory, Gamle Carlsberg Vej 10, DK-2500 Valby, Denmark

**Francisco Palacios**, Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco. Apartado 450. 01080 Vitoria, Spain

**Teresa M.V.D. Pinho e Melo**, Department of Chemistry, University of Coimbra, 3004-535 Coimbra, Portugal

**Matthew Platz**, Chemistry Department, the Ohio State University, Columbus, Ohio, USA

**Philippe Renaud**, University of Bern, Department of Chemistry and Biochemistry, Freiestrasse 3, CH-3012 Bern, Switzerland

**Gloria Rubiales**, Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco. Apartado 450. 01080 Vitoria, Spain

**Jesús M. de los Santos**, Departamento de Química Orgánica I, Facultad de Farmacia, Universidad del País Vasco. Apartado 450. 01080 Vitoria, Spain

**Jean-Pierre Sauvage**, Institut de Chimie, CNRS et Université de Strasbourg, UMR 7177, Laboratoire de Chimie-Organo-Minérale, 4 rue Blaise Pascal, BP 1032, F-67070 Strasbourg cedex, France

**Christine Schilling**, Institute of Organic Chemistry, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6, Karlsruhe, D-76131, Germany

**Werner R. Thiel**, Fachbereich Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Str. Geb. 54, D-67663 Kaiserslautern, Germany

**Christian Tock**, BASF SE, 67056 Ludwigshafen, Germany

**Jérôme Waser**, Laboratory of Catalysis and Organic Synthesis, EPFL SB ISIC LCSO BCH 4306 (Bâtiment de chimie UNIL), CH-1015 Lausanne, Switzerland

**Christian Wenzel Tornøe**, H. Lundbeck A/S, Ottiliavej 9, DK-2500 Valby, Denmark

**Valentin Wittmann**, Fachbereich Chemie, Universität Konstanz, Universitätsstr. 10, D-78457 Konstanz, Germany

# Abbreviations

## Chemical abbreviations, ligands and radicals

Aa	Amino acid
AAE	Azidoacetic acid ethyl ester
ABL	Allegheny Ballistics Laboratory
Ac	Acetyl
acac	Acetylacetonate
ACCN	1,1'-Azobis(cyclohexanecarbonitrile)
AD-mix	Asymmetric dihydroxylation-mix
AIBN	2,2'-Azobisisobutyronitrile
aq	Aqueous
Ar	Aryl
ARC	Accelerated Rate Calorimetry
Asc	Ascorbate
AW-IC	Aza-Wittig reaction/intramolecular cyclization
AW-IEC	Aza-Wittig/intramolecular electrocyclic ring closure
AW-NA-IC	Aza-Wittig/intermolecular nucleophilic addition/intramolecular cyclization
AZT	Azidothymidine
BAM	German Federal Institute for Materials Research and Testing
BEMP	2- <i>tert</i> -Butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine
bmim	1-Butyl-3-methyl-imidazolium
Bn	Benzyl
Boc	<i>t</i> -Butyloxycarbonyl
BPC	Biphenylcarboxylic acid
BPT	Biphenyl tetrazole
Bu	Butyl
Bz	Benzoyl
CAN	Ammonium cerium(IV) nitrate
CASPT2	Complete active space self-consistent field second-order perturbation theory
CASSCF	Complete active space self-consistent field
cat	Catalytic
CB	Cucurbituril

CBS-QB3	Complete Basis Set
Cbz	Carboxybenzyl
CCSD(T)	Coupled-cluster singles and doubles
CD	Cyclodextrin
CD4	Cluster of differentiation 4
CuAAC	Copper(I)-Catalyzed Azide-Alkyne Cycloaddition
DABCO	1,4-Diazabicyclo[2.2.2]octane
DANP	1,3-Diazido-2-nitro-2-azapropane
DATH	1,7-Diazido-2,4,6-trinitro-2,4,6-triazaheptane
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCC	Dicyclohexylcarbodiimide
DCM	CH <sub>2</sub> Cl <sub>2</sub> or dichloromethane
DCR	Dipolar cycloaddition reaction
DEA	Diethylamine
DEAD	Diethyl azodicarboxylate
DFT	Density functional theory
DIAD	Diisopropyl azodicarboxylate
DIBALH	Diisobutylaluminium hydride
DIPEA	Diisopropylethylamine
DLP	Dilauroyl peroxide
DMAP	4-(Dimethylamino)pyridine
DMF	Dimethylformamide
DMPU	1,3-Dimethyl-3,4,5,6-tetrahydropyrimidin-2(1H)-one
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
DNJ	Deoxynojirimycin
DNP	Dioxynaphthalene
DPPA	Diphenylphosphoryl azide
DSC	Differential Scanning Calorimetry
EGA	Evolved Gas Analysis
EPA	Diethyl ether-isopentane-ethanol 5 : 5 : 2
EPR	Electron paramagnetic resonance
ESD	Electrostatic Discharge
ESR	Electron spin resonance
Et	Ethyl
FAB	Fast atom bombardment
Fmoc	Fluorenylmethyloxycarbonyl
FRET	Fluorescence resonance energy transfer
FTIR	Fourier transform infra red
GAP	Glycidyl azide polymer
HEPES	2-(4-(2-Hydroxyethyl)-1-piperazinyl)ethanesulfonic acid
HIV	Human Immunodeficiency Virus
hpyr	1-Hexylpyridinium
IC	Inhibitory concentration
Im	Imidazolyl
KHMDS	Potassium hexamethyldisilazanide

LC	Liquid crystal
LDA	Lithium diisopropylamide
LOVA	Low-vulnerability ammunition
MBQ	Methoxybenzoquinone
<i>m</i> -CPBA	3-Chloroperoxybenzoic acid
Me	Methyl
MIP	2-Methoxy-isopropyl
MMDOc	MMDOC, <i>N,S</i> -dimethyldithiocarbamoyl- <i>N</i> -oxycarbonyl
MMP	Matrix metalloprotease
MOM	Methoxymethyl
MP2	Møller-Plesset
MPDOC	<i>S</i> -Methyl- <i>N</i> -phenyl-1,3-dithiocarbamoyloxycarbonyl
Ms	Mesyl
MW	Microwave/ $\mu$ W
NBS	<i>N</i> -Bromosuccinimide
NHE	Normal hydrogen electrode
NMP	<i>N</i> -Methylpyrrolidone
Ns	2-Nitrobenzenesulfonyl
PEG	Polyethyleneglycol
PEGA	Polyethylene glycolpoly-( <i>N,N</i> -dimethylacrylamide)
PETN	Pentaerythritetranitrate
PFP	Pentafluorophenyl
Ph	Phenyl
PMHS	Poly(methylhydrosiloxane)
PMPA	<i>N,N'</i> -[3-Phenylenebis(methylene)]dipropargylamine
PNA	Peptide nucleic acid
PPG	$\alpha,\omega$ -Bisazidopropylene glycol
PPTS	Pyridinium <i>p</i> -toluenesulfonate
psi	Pound per square inch (1 psi = 6894.75729 pascals)
PT	Phenyl tetrazole
PTOC	1 <i>H</i> -Pyridine-2-thione- <i>N</i> -oxycarbonyl
py	Pyridine
PyBOP	Tradename of benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate
RDX	Research Department Explosive / Royal Demolition Explosive (Hexahydro-1,3,5-trinitro-1,3,5-triazine)
rfx	Reflux
RNA	Ribonucleic acid
ROESY	Rotating Frame Overhauser Enhancement Spectroscopy
scCO <sub>2</sub>	Super critical CO <sub>2</sub>
SEM	[ $\beta$ -(Trimethylsilyl)ethoxy]methyl
SHR	Self-heating rate
STAT3	Signal transducers and activators of transcription 3
TAH	Triazidoheptazine
TAM	Thermal Activity Monitor
TANA	Thioacetamido nucleic acids

TAP	2,4,6-Triazidopyrimidine
TAP-Ac	Triazido pentaerythrite acetate
TASP	Template-assembled synthetic proteins
TAT	<i>trans</i> -Activating transcriptional activator
TBAA	Tetrabutylammonium azide
TBAF	Tetrabutylammonium fluoride
TBAI	Tetrabutylammonium iodide
TBDMS	<i>tert</i> -Butyldimethylsilyl
TBS	Tributylsilyl or <i>tert</i> -butyldimethylsilyl
TBSnA	Tributyltin azide
TEA	Triethylamine
TEMPO	2,2,6,6-Tetramethylpiperidine-1-oxyl
TES	Triethylsilyl
Tf	Trifluoromethylsulfonyl
TFAA	Trifluoroacetic anhydride
TGA	Thermogravimetric Analysis
THF	Tetrahydrofuran
TMDSO	Tetramethyldisiloxane
TMEDA	<i>N,N,N',N'</i> -Tetramethylethylenediamine
TMGA	Tetramethylguanidinium azide
TMS	Trimethylsilyl
TMSA	Trimethylsilyl azide
TNT	Trinitrotoluene
TPP	Tetraphenylporphyrin
Ts	Tosyl
TTF	Tetrathiafulvalene
VEGF	Vascular Endothelial Growth Factor
VEGFR1	Vascular Endothelial Growth Factor receptor 1
YAG	Yttrium aluminium garnet

# **PART 1**

## **Synthesis and Safety**

# 1

## Lab-scale Synthesis of Azido Compounds: Safety Measures and Analysis

*Thomas Keicher and Stefan Löbbecke*

*Fraunhofer Institut für Chemische Technologie ICT, Pfinztal, Germany*

### 1.1 Introduction

More than a century after their discovery organic azides have received renewed interest in synthetic chemistry and are becoming established as an important and versatile class of chemical compounds.<sup>1–3</sup> In particular, in the past two decades an increasing interest in organic azides could be observed due to their vast synthetic utility in conjunction with their easy accessibility via various synthetic routes. Among others, organic azides are currently considered as powerful precursors for reactive species such as nitrenes and nitrenium ions as well as nitrogen-rich compounds such as aziridines, azirines, triazoles, triazolines and triazenes. Moreover, organic azides can be easily transformed into amines, isocyanates and other functional molecules and have more recently received an increasing interest as valuable and versatile reagents within the concept of ‘Click Chemistry’.<sup>4–5</sup>

However, alongside their huge utility in organic synthesis the potential hazardous properties of organic azides must be also carefully taken into account. Organic and inorganic azides are first and foremost energy-rich molecules which often exhibit explosive properties. The azido group is a highly energetic functional group. The  $N_3$   $\pi$ -bond can be easily polarized which consequently results in strong exothermic dissociation reactions under release of molecular nitrogen and reactive nitrene groups. In general, the introduction of an azido group into an organic compound increases its energy content by approx. 290–355 kJ/mol.<sup>6–7</sup> This is one of the reasons why organic azides are considered and partly

used as energetic materials such as energetic polymers or high-energy-density-materials (HEDM) in explosives or propellant formulations.<sup>8-9</sup> However, many organic compounds containing azido groups have not found wide application as practical energetic materials because of their high sensitivity to heat and shock stimuli. This poor thermal and mechanical stability of many organic azides is probably the most crucial property that has prevented chemists in the past from extending their research on azido compounds.

Therefore, in times of increasing worldwide interest in organic azides, it is of utmost importance that their hazardous potential (arising from their energetic and/or toxic properties) and the corresponding safety issues are adequately emphasized. Here, we report on safety precautions and practical measures for the safe handling of azides at laboratory scale. Analytical techniques and other test methods are described that allow characterizing the hazardous potential of organic azides qualitatively and quantitatively at an early stage of small-scale preparation.

## 1.2 Properties that Impose Restrictions on Lab-scale Handling of Azides

### 1.2.1 Hydrazoic Acid and Its Metal Salts

Hydrazoic acid,  $\text{HN}_3$ , and its salts are very poisonous compounds with a toxicity comparable to hydrogen cyanide. Pure hydrazoic acid is a colorless strong-smelling liquid that tends to spontaneous explosion. Because of its high vapour pressure (b.p.  $36^\circ\text{C}$ ) lab-scale handling of  $\text{HN}_3$  is conducted either in water solution or by diluting the acid in organic solvents.

Metal salts of hydrazoic acid from lead, silver, mercury, copper and other heavy metals are very sensitive to mechanical stimulus and explode easily. Heating of these metal azides causes strong explosions. Table 1.1 summarizes some deflagration temperatures of well-known metal azides that decompose explosively when small samples embedded within a metal sleeve are dipped into a hot Wood metal bath.<sup>10</sup> Although these temperatures are relatively high other new metal azide complexes might explode at much lower temperatures.

All heavy metal azides run very quickly into detonation. This specific property has established the use of silver azide and lead azide as primary explosives in detonators.

Remarkably more stable in terms of safe handling are lithium and sodium azide which can be more reliably used in the laboratory since they are hard to initiate explosion by impact or friction. For most laboratory conditions, alkali metal azides are not considered as explosives.<sup>11</sup> However, if ignited or when exposed to strong heat, alkali metal azides decompose rapidly with the evolution of large volumes of nitrogen gas.

**Table 1.1** *Deflagration temperatures of selected metal azides*

Metal azide	Deflagration temperature
Silver azide	$297^\circ\text{C}$
Lead azide	$327^\circ\text{C}$
Mercury azide	$281^\circ\text{C}$
Cadmium azide	$291^\circ\text{C}$

In general, metal azides show an increase in mechanical sensitivity when going from earth alkali metal azides to heavy metal azides which are highly sensitive and explosive. The impact sensitivity of metal azides decreases in the following order:<sup>12</sup>

*Copper > Lead, Mercury > Nickel > Cobalt > Manganese > Barium > Strontium > Calcium > Silver > Thallium > Zinc > Lithium = no explosion*

However, this sequence of impact sensitivities represents only one type of mechanical stability. In case of friction sensitivity (see Section 1.4.2) this order changes. For example, silver azide is approx. 10 times more friction-sensitive than lead azide.<sup>13</sup>

### 1.2.2 Organic Azides

Organic azides are considered as explosives whenever the azido content is remarkably high. Of course, there is no sharp threshold at which the explosive hazard starts. However, as a rule of thumb violent decomposition reactions are expected for azido compounds having a (C + O)/N ratio of <3.<sup>14</sup>

Organic compounds with high azido content are very sensitive to friction and impact, causing strong explosions. For example, cyanuric azide is very sensitive against mechanical stimulus and thus decomposes very easily by detonation. Although the initiation power of this detonation exceeds that of classical primary explosives no technical application has been found so far for this compound due to its high vapour pressure.

Organic azides also show remarkable lower ignition temperatures in comparison to inorganic metal azides. Most of the organic azides decompose at approx. 180 °C.

Some organic azides also show light sensitivity<sup>15</sup> and strong incompatibility with certain chemicals. Several examples have been published where azides exploded when they were brought in contact with sulfuric acid or other compounds.<sup>16-18</sup>

## 1.3 Laboratory Safety Instructions for the Small-scale Synthesis of Azido Compounds

Scientific papers publishing the syntheses of azido compounds usually include in the experimental section certain safety instructions and hints of adequate protection. However, rarely specific instructions for enhancing the safety or detailed methods for protection measures are given.

In general, azido compounds have to be considered and handled as explosive materials. An additional hazard might be caused by their toxicity. In the following the most relevant safety instructions and measures are summarized for the synthesis and handling of azido compounds in the lab:

- Separate the experimental setup with proper shielding and an additional safety screen in the fume hood. Keep the screen of the fume hood always closed during critical operations like heating, distilling and vigorous stirring.
- Safety screens should be made from laminated glass with one or more layers of plastic film embedded between the glass layers. In case of an explosion the broken pieces of glass should remain sticking to the plastic interlayers and not shoot through the laboratory.

- Cover the glassware with adhesive films to reduce the fragmentation in case of explosions, as it is usually done on rotary evaporators and desiccators.
- In addition to the usual protection outfit (lab coat, gloves, safety glasses) wear a face protection shield, ear protection, a leather jacket or a bullet proof vest with arm protection.
- For hand protection use leather gloves (welding type), ideally in combination with steel interwoven Kevlar® gloves! (Klapötke *et al.* have recently published a systematic investigation on the stability of protective gloves against explosion impact. They have found that none of the tested protective gloves could withstand all different kinds of explosion impacts. For example, leather gloves showed best protection against small glass fragments whereas steel interwoven Kevlar® gloves protected well against larger glass splinters.<sup>19</sup>)
- Start the first experiments on a small scale of only a few mg to allow determination of first sensitivity data. Increase the scale only when the scale-up is in accordance with the sensitivity data obtained.
- Keep hazardous azides in solution as long as possible. Solvents desensitize explosives by reducing the sensitivity to mechanical stress.
- Keep solid material wet or soaked with solvent as long as possible. In mixture with liquids explosives are normally desensitized (phlegmatized). Favoured solvents for this purpose are nonflammable solvents like water or halogenated hydrocarbons. Only highly sensitive compounds like primary explosives can detonate without obvious reason even when they are stored under water. It is supposed that these unexpected explosions are caused by internal stress of larger crystals leading to crystal cracks.
- Try to obtain solid products of small particle sizes. Smaller particles/crystals are less sensitive to mechanical stress than larger ones. Only very small particles of  $<10\mu\text{m}$  sometimes show enhanced mechanical sensitivity. Recrystallization experiments should thus be cooled down very quickly under stirring.
- All experiments containing azide compounds that are set up under vacuum should not be vented at elevated temperature. The vent should be remote controlled.
- Do not use metal spatulas because they transfer stronger mechanical stress to the material than spatulas made of wood or Teflon®.
- Keep sufficient distance between the azide material and your body. Do not touch the potential explosive material directly and use, whenever it is possible, gripping devices to manoeuvre the container that encloses the azide compound. Figure 1.1 shows examples of suitable gripping tools. The peak pressure for the explosion decreases at the rate of  $1/R$  for large distances from the explosion centre ( $R$  is the safety distance from the charge). However, when the distance is close to the explosion center, the rate of decrease is between  $1/R$  and  $1/R^2$ . Consequently, in this case the safety distance is a more critical parameter since every small additional distance to the charge will drop the pressure significantly.<sup>20</sup>
- Sensitive explosive azides can be also easily ignited by electrostatic discharge (ESD). Therefore, wear ESD protective clothing (or at least cotton clothes) and antistatic shoes. The laboratory floor should be ESD conductive or there should be at least static dissipative mats (ESD mats) installed in front of the fume hood where the azides will be synthesized and handled.
- Apart from all mentioned energetic hazards, the synthetically working chemist must also keep in mind the toxic nature of azides!



**Figure 1.1** Examples for gripping devices

## 1.4 Analyzing Safety-related Properties of Azides

Because of the described hazardous potential of organic azides the analysis of their safety-related properties is of utmost importance to ensure safe synthesis and subsequent processing. Unfortunately, in literature only very few data can be found describing thermal properties of organic azides. Data on impact, friction or ESD sensitivity are also mostly not available as well as any reliable information on (long-term) stability and energy content. One of the reasons for these missing data might be that most scientific reports on organic azides are provided by research groups focusing on the preparation and subsequent conversion of organic azides. One can assume that the specific analytical techniques that are required to measure all relevant safety-related properties are not fully available in these synthesis labs.

Therefore, in the following we describe the most important and relevant analytical methods and characterization techniques that are required to evaluate the hazardous potential of organic azides qualitatively and quantitatively. From our experience, it is essential to conduct sensitivity tests, thermoanalytical measurements and stability tests of energy-rich compounds at an early stage of every small-scale preparation. Naturally, such safety analysis is mandatory for the synthesis of new organic azides to decide whether the scale of synthesis can be enlarged and subsequent processing of this new compound is possible in a safe manner. Moreover, we strongly recommend conducting permanent safety analyses also for such energy-rich azides whose syntheses have already been established in the labs. Slight differences in the experimental procedure might result in products of different heat/shock sensitivity and stability, for example due to different particle sizes and crystal morphologies. Consequently, sensitivity and stability data of an energetic azide must be strictly rechecked after each synthesis campaign.

### 1.4.1 Impact Sensitivity Testing

The impact sensitivity of energetic compounds is tested with a so-called fall hammer equipment. Samples are exposed to the impact of falling weights from variable heights

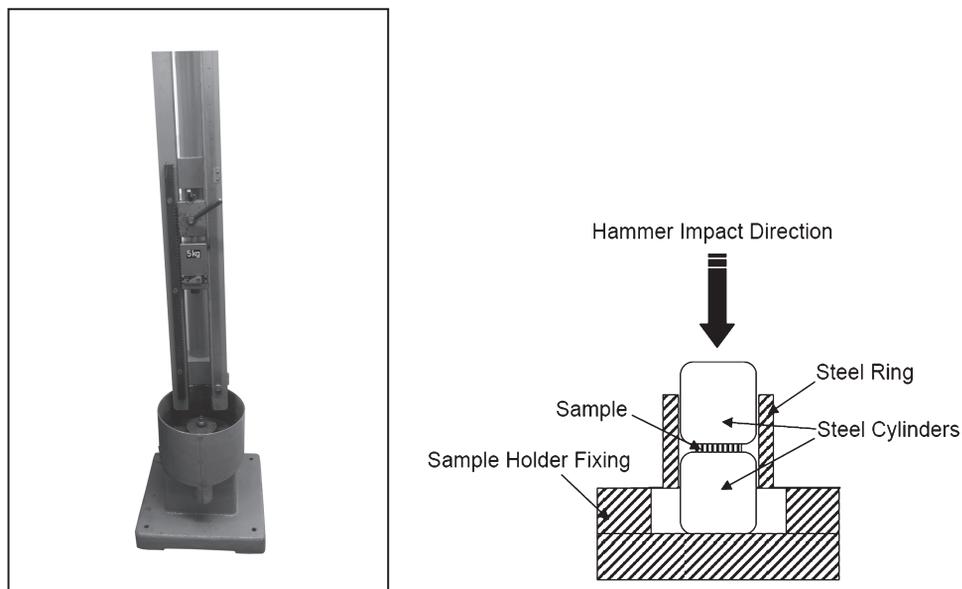
and the measured sensitivity parameter is the height at which the samples decompose or explode. There are different types of fall hammer systems and corresponding test procedures in operation all over the world.<sup>21–24</sup> The main difference between them is in the design of the sample holders or sample confinements. Other differences are the amount of samples that are used for the tests, the type of drop weight and the number of recorded decompositions/explosions that have to occur at a certain height to produce a positive result. Unfortunately, the different test procedures define positive results not in the same way. Some tests describe positive impact sensitivity by the height where at least one of the six (or sometimes ten) samples could be initiated; other tests determine the height where 50% of at least 20 samples are initiated. As a consequence, results from different fall hammer systems might deliver different results. Moreover, for new upcoming energetic materials sometimes different impact sensitivity values are reported although tests were conducted by using the same type of fall hammer but were operated by different laboratories. These varying sensitivity data might be either caused by different sample qualities (purity, particle size, crystal density, liquids with/without gas bubbles that act as ‘hot spots’, etc.<sup>24–26</sup>) or by different operators of the test system. In case of strong explosions initiation can be easily recognized, but sometimes the decomposition of the sample starts with weak smouldering, which is hard to notice for the operator of the fall hammer system. Consequently, to obtain a more reproducible detection level for positive responds some laboratories use microphones to measure the explosion bang during impact sensitivity tests.<sup>22,27–30</sup>

In literature, there are several attempts described to predict and calculate the impact sensitivity of energetic materials.<sup>28,31–38</sup> Most of these papers deal only with nitro- and nitrate ester compounds, whereas the impact sensitivity of azides has not been the subject of detailed calculations so far, apart from recently published structure-sensitivity correlations on inorganic azides.<sup>39</sup>

Figure 1.2 shows the set-up of the fall hammer equipment as it has been defined by the German Federal Institute for Materials Research and Testing (BAM).<sup>40</sup> There are two versions of different sizes in operation. The small fall hammer is for testing sensitive explosives such as primary explosives and is operated with weights up to 1 kg. The large hammer is used for more insensitive explosives that can be impacted by hammer weights of 1.5 and 10 kg. The test sample has a volume of 40 mm<sup>3</sup> and it is placed between two steel cylinders that are fixed by a steel ring (Figure 1.2). The cylinders have a diameter and a height of 10 mm and are made from ground and hardened steel. The reported impact sensitivity value is the fall energy, given in Nm, at which at least one sample from a series of six has been initiated.

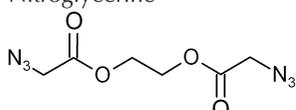
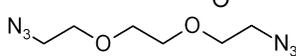
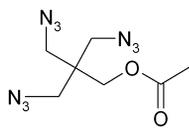
In Table 1.2 impact sensitivity values of different azido compounds according to the BAM fall hammer procedure are listed and compared with the corresponding values of the well-known explosives trinitrotoluene (TNT) and nitroglycerine. For the BAM procedure it is necessary to have at least one positive event within a series of six trials (probability of at least 16.7%). In the case of the US drop hammer tests (according to the Bruceton procedure) the required probability level is often 50% initiation within a series of at least 25 trials.

Therefore, the impact sensitivity of an energetic compound is not a strictly fixed absolute value like its melting point but is subject to certain fluctuations depending on the sample characteristics, the test equipment and testing procedure as well as the operator. However, impact sensitivity values provide clear safety information and can be used in practice in particular as a comparative method.



**Figure 1.2** BAM fall hammer set-up (left) and corresponding sample holder (right)

**Table 1.2** Impact sensitivity values of selected azide compounds compared with trinitrotoluene and nitroglycerine

Explosive	Fall hammer weight / kg	Fall height / m	Impact sensitivity (BAM procedure) / Nm
Lead azide <sup>24</sup>	5	0.15	7.5
Trinitrotoluene <sup>24</sup>	5	0.30	15
Nitroglycerine <sup>24</sup>	0.1	0.20	0.2
	5	0.1	5
	1	0.2	2
	0.1	0.2	0.2

### 1.4.2 Friction Sensitivity Testing

For measuring and testing the friction sensitivity, samples of energetic compounds are exposed to friction forces that are generated by different setups and methods.<sup>22–24,41</sup> In the ABL (Allegheny Ballistics Laboratory) Sliding Friction Test the sample is pressed by a steel roll with an adjustable force on an anvil which is accelerated by the impact of a

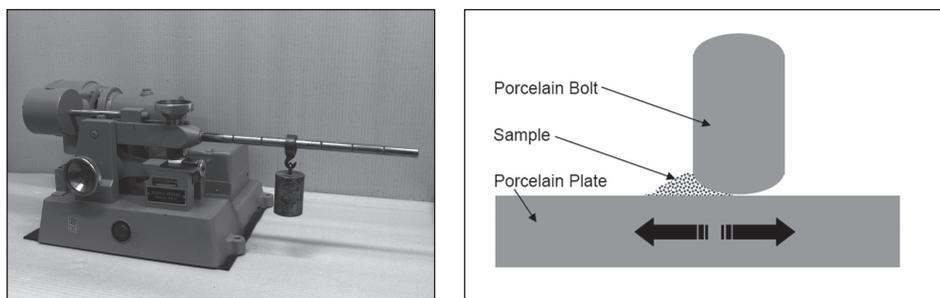
pendulum. The measurement of the compressive force is done when from 20 samples 50% are initiated. In another setup developed by the Bureau of Mines, a pendulum with different shoes (steel or fibre reinforced plastic) grazes over the sample (7 g) that is spread on an anvil with three grooves. This test is passed when 20 trials are not giving any initiation.

In the Roto-Friction Test developed at the American Naval Surface Warfare Center a friction rod is rotating on the sample that is placed into a recess bored sample holder. The normal force weights that press the friction rod on the sample can be varied and torque measurement equipment records the force transmitted through the sample to the sample holder. The friction energy value is calculated from the measured torque and from the exposure time that the sample is stimulated by rotating friction till any decomposition or explosion occurs.

The friction test setup defined by the German Federal Institute for Materials Research and Testing (BAM) measures the sensitivity of samples that are exposed to a friction stimulus generated between two roughened porcelain surfaces.<sup>40</sup> 50 mg of a sample resting on a porcelain plate is stimulated by a porcelain pin with adjustable down-pressing force. For stimulation, the sample table is driven by a motor horizontally forwards and backwards for one full cycle of reciprocating motion. Figure 1.3 shows the setup of the BAM friction test.

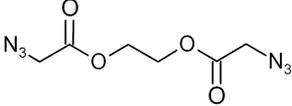
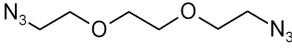
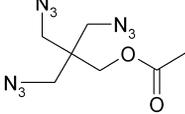
There are two versions of the friction test apparatus in operation, a standard size apparatus and a small size version. The small device is particularly designed to test sensitive materials such as primary explosives. It can be operated with different weights on the porcelain bolt holder allowing loads in the range of 0.1 to 10 N. On the standard BAM friction test apparatus higher forces on the pin varying from 5 to 360 N can be applied.

The results obtained by the BAM friction test refer to the smallest load on the pin under which deflagration, crackling or explosion of the sample is observed, at least once in six consecutive trials. Other test procedures provide friction energy values on the basis of a 50% initiation probability. Therefore, absolute friction sensitivity values that are measured might be subject to certain fluctuations depending on the specific properties of a sample (e.g. purity, particle size, etc.) and the test equipment used. Nevertheless, friction sensitivity measurements provide useful safety information and allow direct comparison with other sensitive or less sensitive materials, and are thus of the same importance as impact sensitivity data.



**Figure 1.3** BAM friction test apparatus (left) and scheme of the measuring principle (right)

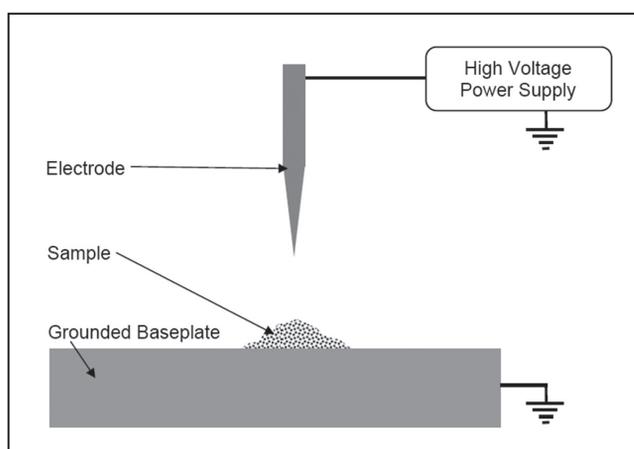
**Table 1.3** Friction sensitivity values of selected azide compounds compared with TNT and nitroglycerine

Explosive	Friction sensitivity (BAM procedure) / N
Lead azide <sup>24</sup>	0.1
TNT <sup>24</sup>	up to 360 no reaction
Nitroglycerine <sup>24</sup>	up to 360 no reaction
	128
	128
	84

In Table 1.3 exemplary friction sensitivity values of azido compounds according to the BAM procedure are listed and compared with the corresponding values of TNT and nitroglycerine. A comparison with the sensitivity values listed in Table 1.3 points out that the sensitivity to friction and impact of a specific energetic compound might differ significantly.

### 1.4.3 ESD Testing

In electrostatic discharge (ESD) tests, the amount of energy that is required to ignite explosives by electrostatic stimuli is determined. Most explosives have low electrical conductivity. Therefore, the potential of the electrostatic pulse has to be high to generate a sparkover. Figure 1.4 illustrates the principle setup of an ESD testing device.

**Figure 1.4** Schematic setup of an ESD testing apparatus

First, a capacitor is charged up to a high voltage level followed by the release of the electric energy via a discharge pole through the sample which is placed on an earthed plate or pole. Samples are tested by varying the intensity of the released electrostatic discharge. A positive result is defined whenever a flash, spark, burn, or specific noise is detected.

There are different ESD test systems and procedures in worldwide operation.<sup>22–23,42–44</sup> Main differences are in the design of the sample holder, the size and shape of the discharge electrode, the voltage level before discharge and the number of experiments that are required to define a positive or negative ESD test result. Consequently, different ESD sensitivity values can be found in literature for the same energetic compound. Besides the influence of different ESD test apparatus the actual constitution of a sample has mostly a more significant impact on its ESD sensitivity. For example, it is well known that differences in particle size, grain shape, temperature and moisture content provide different ESD sensitivity values.<sup>13,23,45–49</sup>

In Table 1.4 exemplary ESD test results are listed that are reported for different energetic materials including inorganic azides (no comparable data are available for organic azides). It can be clearly seen that different test setups give different sensitivity values for the same material. Tremendous differences arise when samples of different particle size are tested. As expected, smaller particles are more sensitive to electrostatic ignition than larger ones. Another parameter that influences the ESD test result is the confinement of the sample. Fine powders are more sensitive to electrostatic ignition in the unconfined state and coarse material gets more sensitive if it is exposed to the electrostatic discharge in the confined state.

These partly huge fluctuations in ESD sensitivity of energetic compounds arising from different sample constitutions should sensitize every person practically working with energetic compounds like organic azides in the lab. One person can store up to 100 mJ by wearing insulating shoe soles in a dry environment. The maximum electrostatic discharge energy in a spark is up to 20 mJ and is thus high enough to initiate sensitive materials.<sup>50</sup>

**Table 1.4** Exemplary ESD test results for some azide compounds and other energetic materials

Sample	50% ignition probability at varied voltage / mJ (according to <sup>45</sup> )	Zero ignition probability at 5000 volts / mJ (according to <sup>46</sup> )	
		Unconfined sample	Confined sample
Lead azide	0.06	7	7
Lead azide/dextrin	23 / 112 <sup>a</sup>	n.a.	n.a.
Lead azide/dextrin	23	n.a.	n.a.
Sodium azide	>79,433	n.a.	n.a.
TNT	22,387	62 / >11,000 <sup>b</sup>	4,380 / 4,680 <sup>b</sup>
PETN	2,630	62 / >11,000 <sup>b</sup>	210
Black powder	2,692 / 4,074 <sup>b</sup>	>12,500	800

<sup>a</sup>two different ESD test devices;

<sup>b</sup>different particle sizes; n.a.: not available.

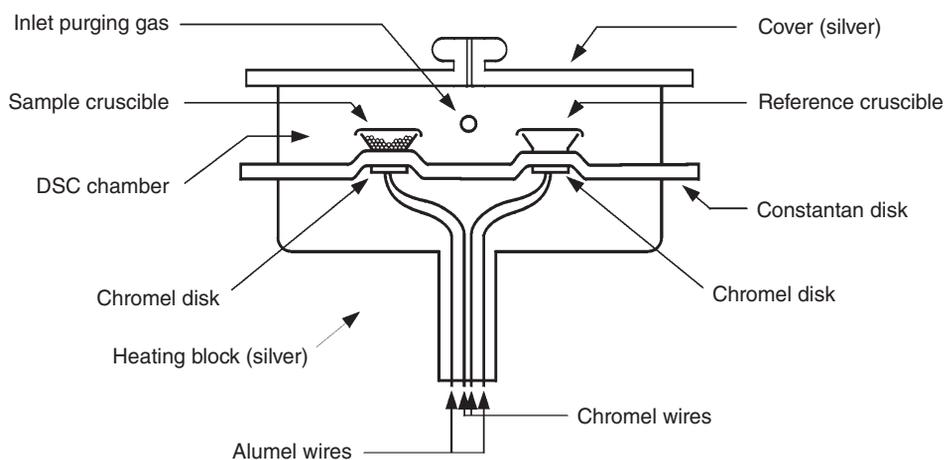
### 1.4.4 Thermoanalytical Measurements

In addition to measuring the mechanical and electrical sensitivity of energetic compounds it is essential to also analyze their thermal and caloric properties thoroughly. In particular, the data on the thermally induced decomposition behavior are required to evaluate the hazardous potential of energy-rich compounds such as organic azides.

In thermal analysis, physical parameters like mass, heat flow, heat capacity and enthalpy are measured as a function of temperature and time, while the sample is subjected to a controlled temperature programme (which in most cases is the application of linear heating rates or isothermal conditions).<sup>51–53</sup> The two most common thermoanalytical techniques to investigate thermal and caloric properties of energy-rich compounds are Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA).

Differential Scanning Calorimetry (DSC) is a technique for measuring the energy necessary to establish a nearly zero temperature difference between a sample and an inert reference material, as the two specimens are subjected to identical temperature regimes in an environment heated or cooled at a controlled rate. Two different types of DSC instruments are known: power-compensation DSC and heat-flux DSC.<sup>54</sup> In power-compensation DSC the temperatures of the sample and reference are controlled independently using separate, identical furnaces. Both, sample and reference are kept at an identical temperature by varying the power input to the two furnaces; the energy required to do this is a measure of the enthalpy or heat capacity changes in the sample relative to the reference.

Today, heat-flux DSC is more commonly used. Here, sample and reference are connected by a low-resistance heat-flow path which is mostly a metal disc. This assembly is enclosed into a single furnace. Enthalpy or heat capacity changes in the sample cause a difference in its temperature relative to the reference. The temperature difference and thus the resulting heat flow are recorded and related to enthalpy changes in the sample. Figure 1.5 shows a schematic cross-section of a typical heat-flux DSC cell. The sample (up to

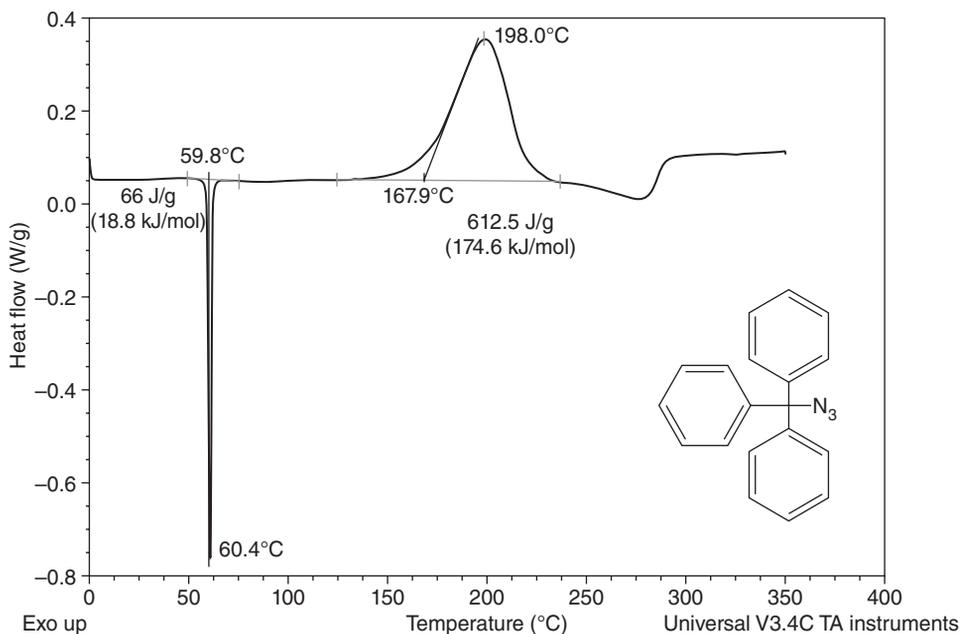


**Figure 1.5** Schematic setup of a heat-flux DSC cell (DSC 2920, TA Instruments Inc.)

several mg) is placed in a small crucible (for example, an aluminum pan). In most cases an empty crucible is used as reference sample. The entire DSC cell can be permanently purged by inert or reactive gases. In case of analyzing energetic materials, argon or nitrogen gas is usually used to remove volatile substances and decomposition gases during the measurement. In case of azido compounds the use of argon is recommended since nitrogen is also one of the decomposition products. Samples that are expected to exhibit strong exothermic decomposition are usually analyzed in non-hermetically sealed crucibles to avoid uncontrolled pressure built-up and allow decomposition gases to be released (in most cases aluminum pans with pierced lids are employed). Moreover, small sample sizes of partly <1.0mg are used and only slow heating rates up to 5.0K/min are applied to avoid uncontrolled decomposition.<sup>55</sup>

In general, DSC measurements allow the recording of all types of chemical and physical transformations of a sample that involve exothermic and endothermic processes or changes in heat capacity.<sup>54</sup> In particular, exothermic decomposition reactions as well as endothermic phase transitions (melting, boiling, sublimation, solid-solid phase transition between different crystal morphologies, and glass transition of polymers) are the most relevant processes which are considered in energetic materials analysis. DSC measurements provide both, the characteristic temperature values of all endothermic and exothermic processes (onset temperature, peak temperature) and the corresponding enthalpies.

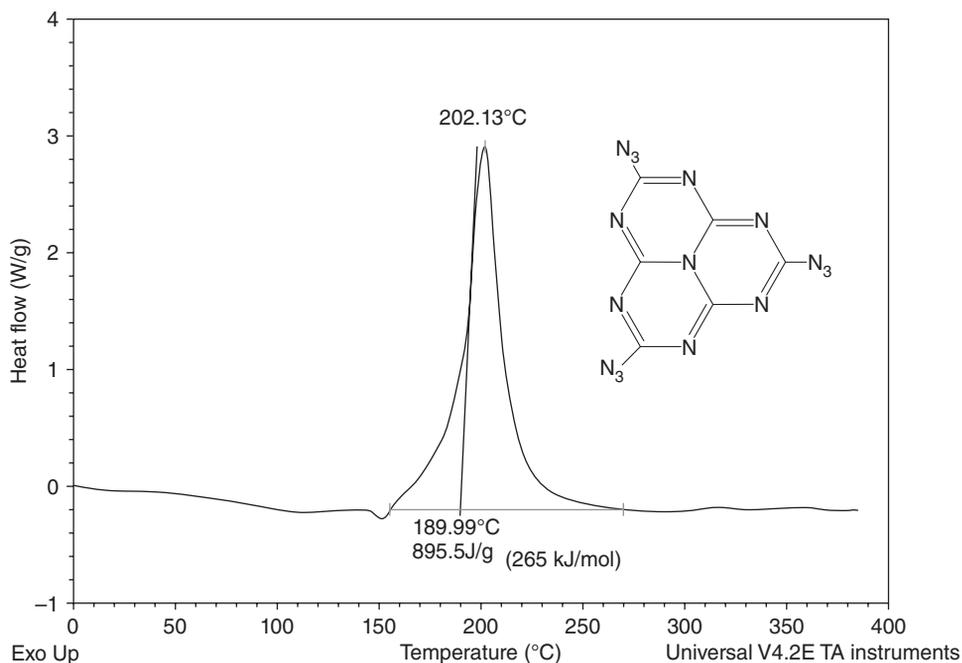
As an example, Figure 1.6 shows the DSC measurement of triphenylmethyl azide (trityl azide) applying a linear heating rate of only 1.0K/min (sample size: 3.35 mg, Argon atmosphere, Al pan with pierced lid). Endothermic processes are displayed by negative



**Figure 1.6** DSC measurement of triphenylmethyl azide (1.0K/min, 3.35 mg, open Al pan)

heat flow values, whereas exothermic processes show a positive heat flow. Three main processes can be identified in the DSC graph of trityl azide. First, a sharp endothermic melting peak occurs at a calculated onset temperature of 59.8 °C (peak maximum at 60.4 °C). The melting enthalpy, calculated from the integral of the melting peak, is approx. 18.8 kJ/mol (66 J/g). Further heating of trityl azide leads to its exothermic decomposition starting at approx. 150 °C. However, the calculated onset temperature of the decomposition is 168 °C and the peak maximum temperature is 198 °C. The decomposition enthalpy under the chosen experimental conditions is 174.6 kJ/mol (612.5 J/g), which is already remarkable but not hazardous. Finally, after completion of the exothermic decomposition, a huge endothermic process can be observed, which can be assigned to the slow sublimation of decomposition products.

Besides temperature and enthalpy values DSC measurements provide additional safety-related information on the strength and intensity of decomposition reactions. In particular the steepness and width of the exothermic decomposition peaks are qualitative indicators for reactivity and thus vehemency of the thermally induced decomposition reaction. As an example, Figure 1.7 shows the DSC curve of 2,5,8-triazido-s-heptazine (TAH),<sup>9,56</sup> a nitrogen-rich energetic compound, recorded at a linear heating rate of 5.0 K/min (argon atmosphere, Al pan with pierced lid). A sample mass of only 0.71 mg was used to detect the strongly exothermic decomposition at a calculated onset temperature of 190 °C. The steep and relatively narrow exothermicity indicates a more vehement decomposition in



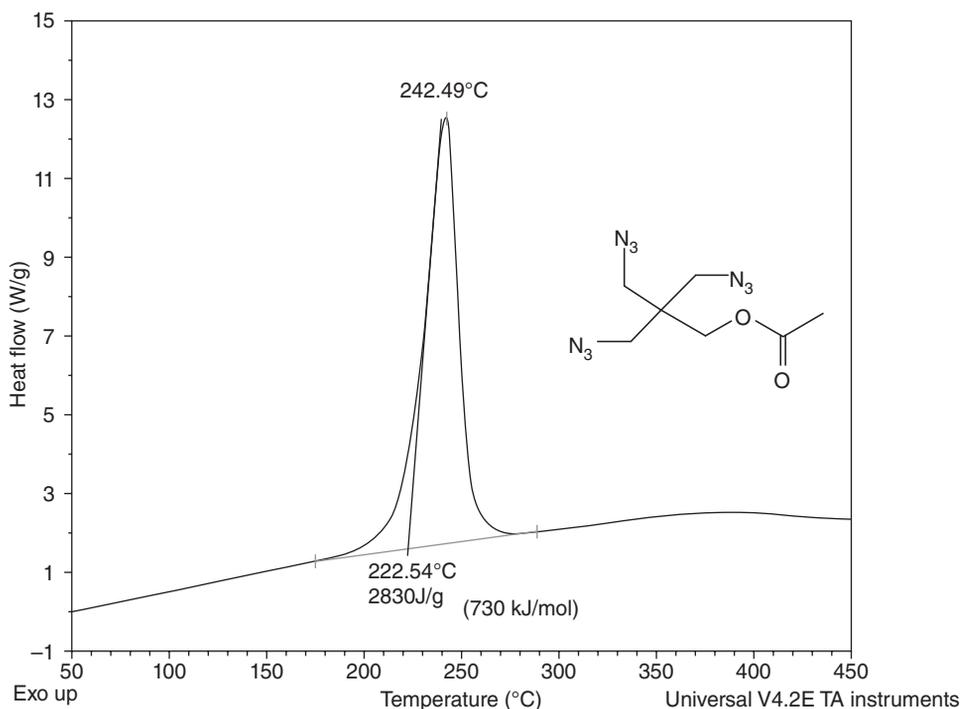
**Figure 1.7** DSC measurement of 2,5,8-triazido-s-heptazine (TAH) (5.0 K/min, 0.71 mg, open Al pan)

comparison to the previous example by releasing 265 kJ/mol under the chosen experimental conditions.

Almost threefold the amount of heat is released by a sample of triazido pentaerythrite acetate (TAP-Ac<sup>57-58</sup>), confined in a hermetically sealed aluminum pan; its DSC measurement is shown in Figure 1.8. A small sample of only 0.35 mg was analyzed applying a linear heating rate of 5.0 K/min. The DSC graph shows no phase transition or any other transformation of TAP-Ac until decomposition starts at approx. 190 °C (calculated onset temperature: 222 °C). A steep increase in heat flow combined with a narrow exothermic peak is a clear indication for a violent and rapid decomposition of TAP-Ac. In fact, a high decomposition enthalpy of approx. 730 kJ/mol was measured under the chosen experimental conditions.

TAP-Ac is a good example to emphasize the importance of thoroughly analyzing the hazardous potential of energy-rich compounds. In spite of its three azido groups TAP-Ac shows a surprisingly high stability over a wide temperature range in DSC experiments. This makes one believe that TAP-Ac is a thermally stable and thus nonhazardous compound under ambient conditions. However, in huge contrast to its thermal robustness fall hammer tests of TAP-Ac have revealed its high impact sensitivity of only 0.2 Nm (see Table 1.2).

In many laboratories DSC measurements of energetic materials are complemented by *Thermogravimetric Analysis (TGA)*. In TGA experiments the sample mass is recorded

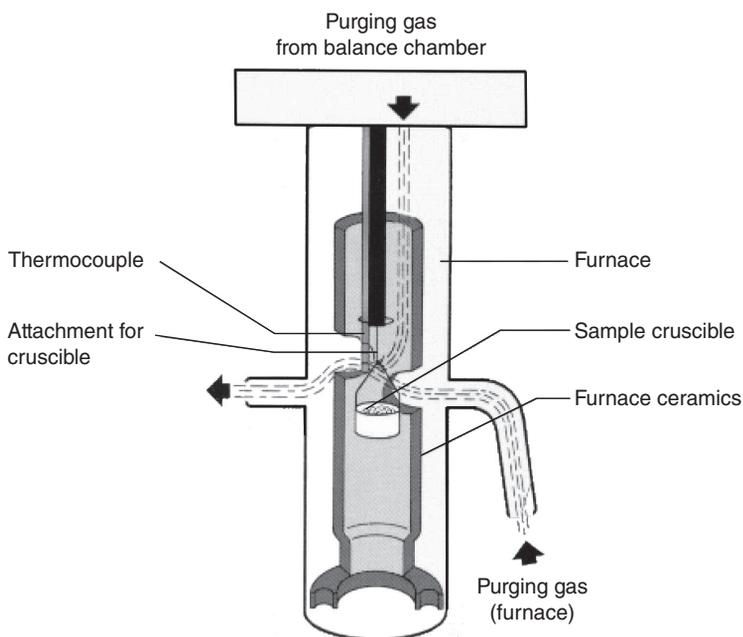


**Figure 1.8** DSC measurement of triazido pentaerythrite acetate (TAP-Ac) (5.0 K/min, 0.35 mg, sealed Al pan)

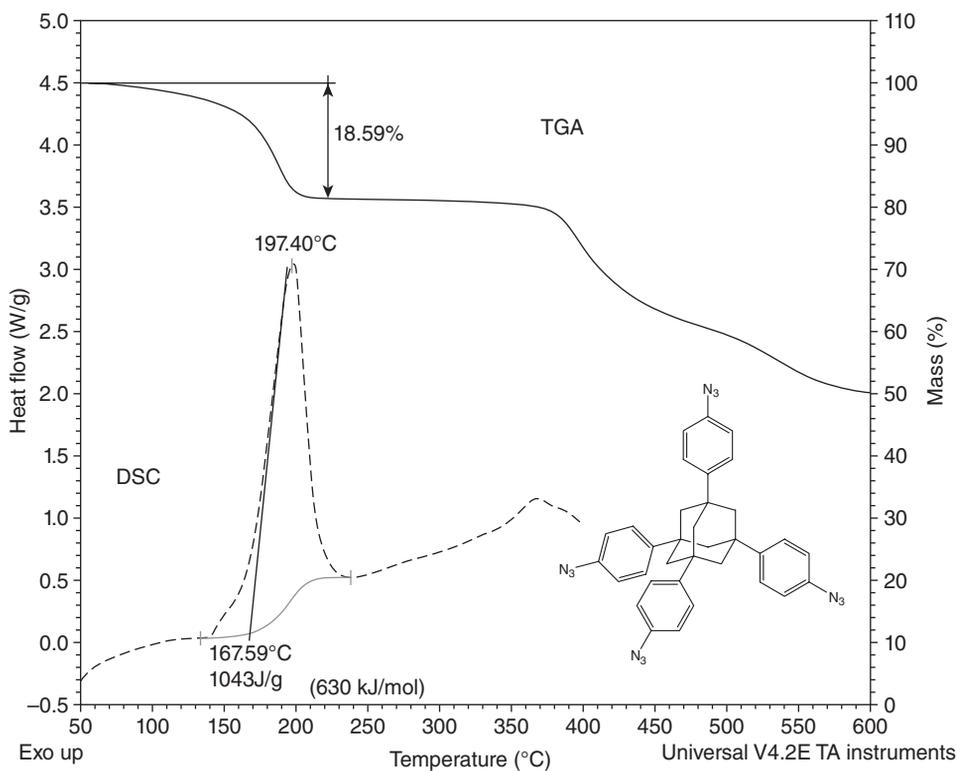
as a function of temperature and time while the sample is subjected to a linear heating rate or an isothermal treatment.<sup>51</sup> The samples (up to several mg) are filled into an open crucible made of platinum or alumina which is attached to the arm of a recording microbalance, the so-called thermobalance. The sample is heated in a temperature-controlled furnace according to a pre-programmed temperature/time profile. During the experiment both the furnace and the thermobalance are purged independently with inert gas (usually argon or nitrogen). Figure 1.9 shows schematically a typical setup of a TGA furnace.

Since the mass changes of a sample are recorded in TGA experiments, the method is predominantly used to investigate the thermal decomposition behavior of compounds. It typically provides information on the decomposition onset temperature and the mass loss that occurs during the decomposition reaction. TAP-Ac, for example, degrades completely during its strongly exothermic decomposition forming only gaseous products within one total mass loss step. However, other energetic azides degrade stepwise.<sup>59</sup> For example, Figure 1.10 shows the DSC and TGA data of 1,3,5,7-tetrakis(4-azidophenyl)adamantane, a recently synthesized compound.<sup>60</sup> The organic azide decomposes stepwise during slow heating at 5.0 K/min. However, the main exothermicity of the thermal decomposition (as measured by DSC) is related only to the first mass loss step of 18.59% which corresponds well with the release of four equivalents of molecular nitrogen.

This example also shows that the combined use of different thermoanalytical methods allows a more detailed analysis of decomposition processes. Moreover, whenever DSC and TGA are combined with *Evolved Gas Analysis (EGA)* – which allows an in-situ



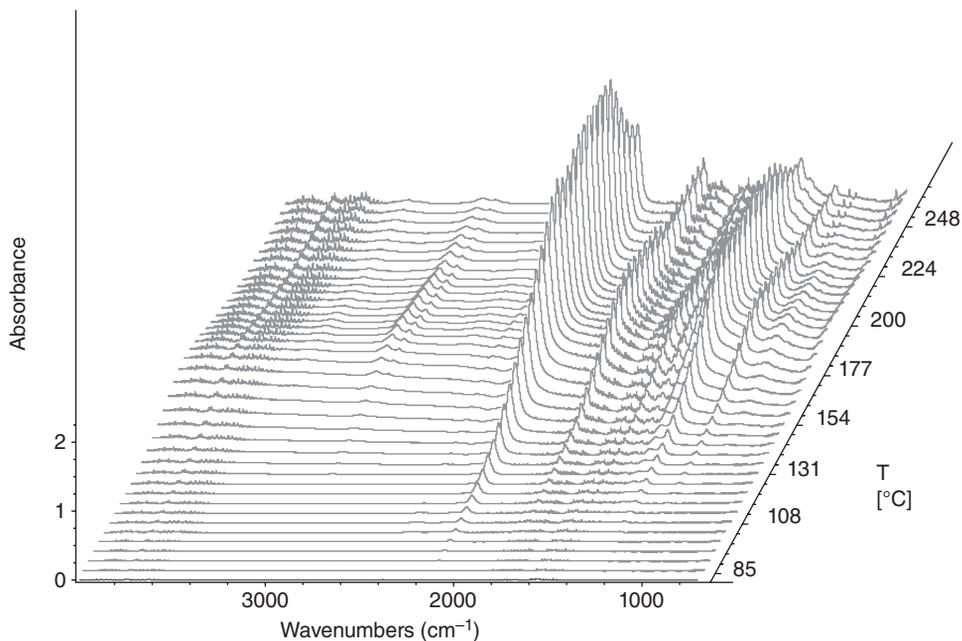
**Figure 1.9** Schematic setup of a TGA cell (TGA 2950, TA Instruments Inc.)



**Figure 1.10** DSC and TGA measurement of 1,3,5,7-tetrakis(4-azidophenyl)adamantane (DSC: 5.0K/min, 1.05mg, open Al pan; TGA: 5.0K/min, 0.89mg, Pt pan)

detection of gaseous decomposition products by infrared spectroscopy or mass spectrometry – chemical pathways and mechanisms of thermal decomposition can be revealed.<sup>51,61</sup> As an example, Figure 1.11 shows the infrared spectroscopic detection of decomposition gases during the linear heating of 4.0mg TAP-Ac at 5.0K/min. The EGA waterfall-plot illustrates the temperature-resolved release of carbon dioxide (characteristic infrared absorption bands at  $2360\text{ cm}^{-1}$ ,  $2322\text{ cm}^{-1}$ , and  $700\text{ cm}^{-1}$ ), water (broad absorption centered at  $3750\text{ cm}^{-1}$  and  $1600\text{ cm}^{-1}$ ) and methyl acetate ( $2964\text{ cm}^{-1}$ ,  $1778\text{ cm}^{-1}$ ,  $1450\text{ cm}^{-1}$ ,  $1375\text{ cm}^{-1}$ ,  $1247\text{ cm}^{-1}$ , and  $1050\text{ cm}^{-1}$ ) as well as the formation of traces of ammonia (double band at  $965$  and  $931\text{ cm}^{-1}$ ) in subsequent gas phase reactions (Note: molecular nitrogen is also a main decomposition product of TAP-Ac that, however, cannot be detected by infrared spectroscopy but by mass spectrometry in coupled TGA-MS setups.) From the individual gas evolution profiles kinetic data can be derived as they can be also obtained from DSC and TGA experiments conducted under different heating rates.

In conclusion, thermoanalytical methods are powerful tools to determine safety-related thermal properties of azides. Whenever possible, we strongly recommend performing DSC measurements of potentially energetic azides as soon as a few milligrams of substance are available. The combination of DSC data on decomposition temperature and



**Figure 1.11** Infrared spectroscopic Evolved Gas Analysis of triazido pentaerythrite acetate (TAP-Ac) (5.0K/min, 4.0mg, open Al pan)

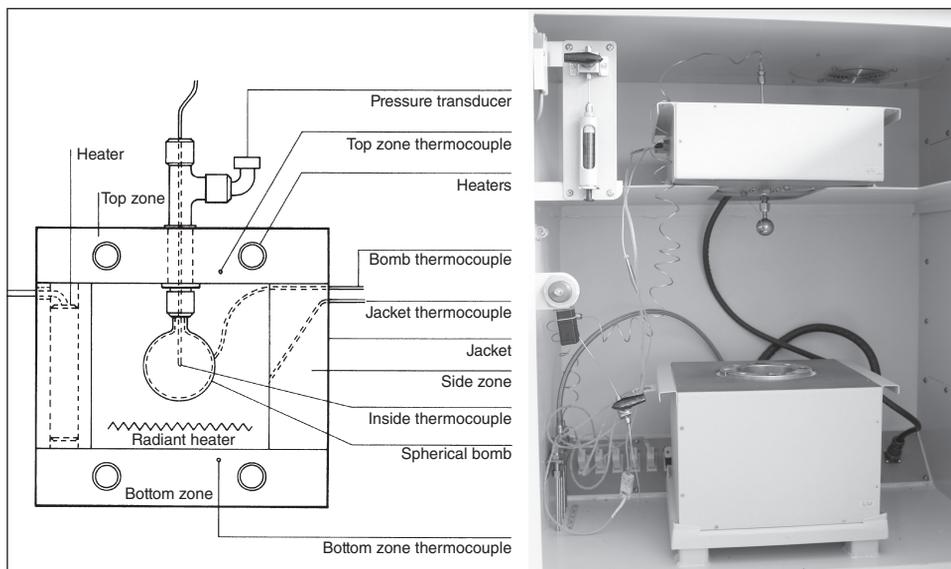
enthalpy with data on mechanical and electrical sensitivity will provide a first safety evaluation on the basis of small sample sizes.

#### 1.4.5 Calorimetric and Gravimetric Stability Tests

So far, analytical methods and characterization techniques have been described which provide relatively fast information on the shock, temperature and heat sensitivity of energetic compounds. However, besides the short-term sensitivity to temperature and heat as measured by thermoanalytical techniques, also the mid- and long-term sensitivity and stability of energetic compounds must be considered. In particular, stability becomes an important safety issue whenever energetic compounds like azides are stored in larger quantities for further processing.

Therefore, gravimetric and different calorimetric methods have been established to investigate stability and aging behavior of energetic compounds.<sup>62–64</sup> Here, mass loss tests and the analysis by adiabatic and isothermal heat flow calorimetry are briefly described.

*Mass loss tests* of solid energetic materials are carried out under isothermal conditions in precise temperature controlled furnaces. Usually, samples of 1–2 g are stored in special, open sample tubes at 75 °C or 90 °C for at least 18 days. During this period the sample mass is constantly recorded. A mass loss of >3% after 18 days at 90 °C is usually an indicator for restrictions in long-term stability. However, stability standards are only specified for specific energetic materials and compositions. For example, stable nitrocellulose-based propellants have to exhibit a mass loss of <2% after 18 days storage at 90 °C.<sup>65</sup> Mass loss data of energetic azides have been only rarely published so far. Only



**Figure 1.12** Setup of an accelerating rate calorimeter (Thermal Hazard Technology, GB)

few data are available for azido polymers which are used as binders or plastizisers in propellant formulations.<sup>66</sup>

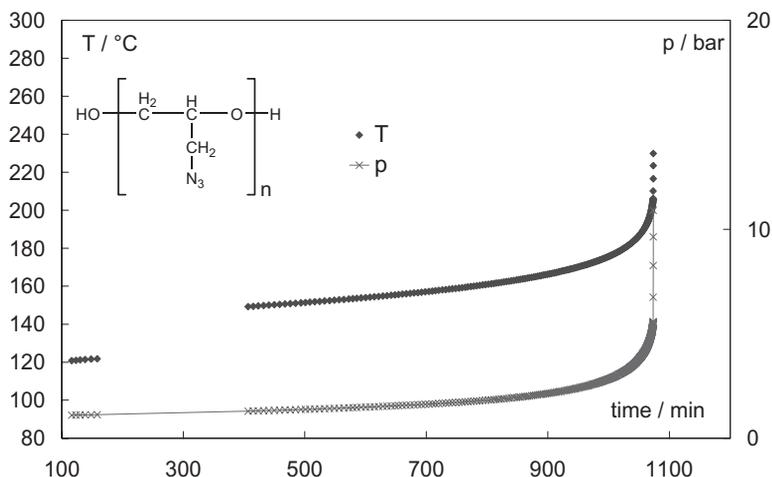
Other techniques to investigate the thermal stability of energetic materials are employing calorimetric methods. For example, adiabatic self-heating of samples is measured by *Accelerating Rate Calorimetry (ARC)*.<sup>64,67–69</sup> In ARC experiments a sample is placed in a spherical metal cell of 10 cm<sup>3</sup> volume which may hold several grams. The sample cell is mounted in the center of a well-isolated furnace whose temperature is precisely adjusted and controlled. Figure 1.12 shows a typical ARC setup. Pressure within the cell can be monitored during the measurement via a direct connection to an external pressure sensor (pressure range: 1–200 bar). Adiabatic conditions are realized by adjusting the furnace temperature to the temperature of the sample. This allows an active control of potential heat losses.

The ARC system is often operated in a stepwise ‘heat-wait-search’ modus. After heating to a certain temperature, the system is stabilized for a pre-defined time until the calorimeter starts seeking for a temperature increase caused by first decomposition processes. If the temperature increase surpasses a pre-defined threshold (e.g. 0.01 K/min) the furnace temperature follows the sample temperature in the adiabatic mode and the calorimeter tracks the adiabatic temperature rise due to the self-heating of the sample. If the threshold is not surpassed after a certain period of time, the calorimeter proceeds with the next temperature step. In comparison to DSC analysis ARC measurements are significantly more sensitive, usually by a factor of 100 or more. Sensitivity is as low as 0.5 mW/g and self-heating rates of 0.01 K/min can be detected.

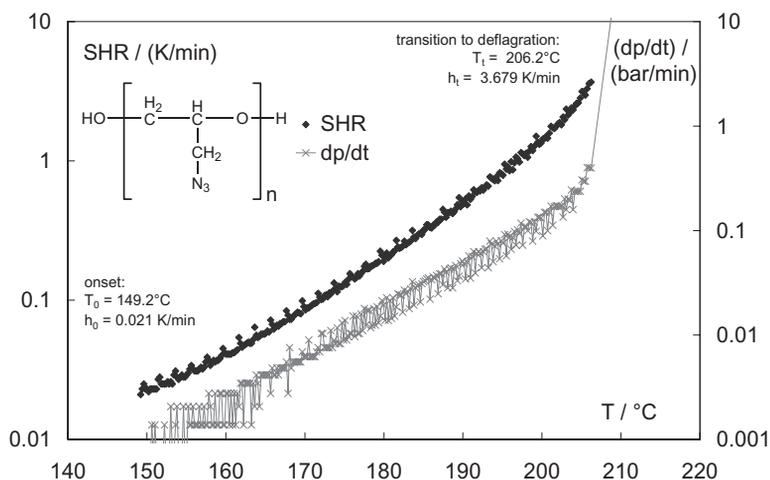
The most relevant safety and stability information obtained from ARC experiments are the self-heating rate, the pressure rate and the adiabatic temperature rise of energetic materials as a function of temperature. As an example, Figures 1.13 and 1.14 show such

data for GAP diol, an energetic glycidyl azide polymer based on polyether diol and grafted with energetic azido groups in the polymer chain. The ARC measurement confirms the overall good stability of the polymer showing a transition to deflagration at  $>200^{\circ}\text{C}$ .<sup>66,70</sup>

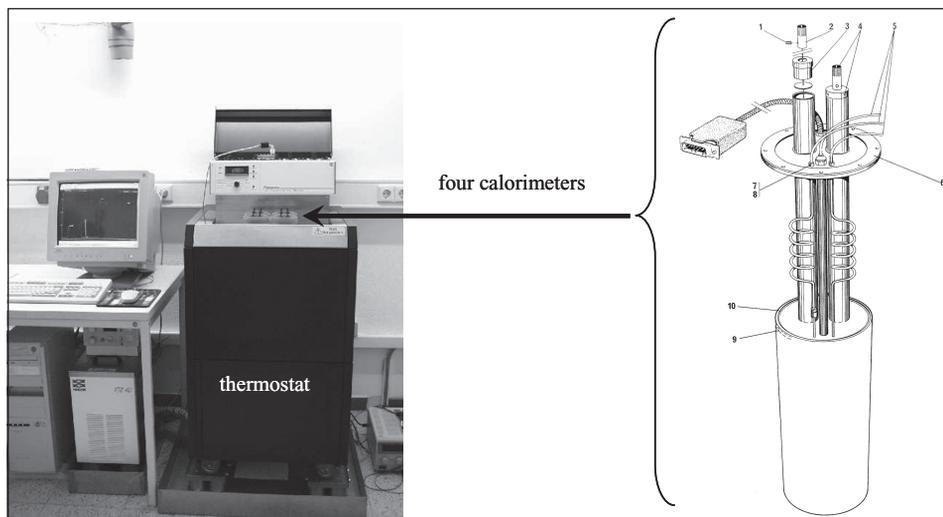
Another highly sensitive calorimeter is the *Thermal Acitivity Monitor (TAM)*, an isothermal heat flow calorimeter which was originally developed for the investigation of biological systems.<sup>71-72</sup> The thermal acitivity monitor is a differential calorimeter working with reference samples. It measures heat flows induced by slow decomposition reactions of samples stored under precisely controlled isothermal conditions. The high sensitivity



**Figure 1.13** ARC measurement of GAP diol: self-heating until deflagration



**Figure 1.14** ARC measurement of GAP diol: self-heating rate (SHR) and pressure rate until deflagration

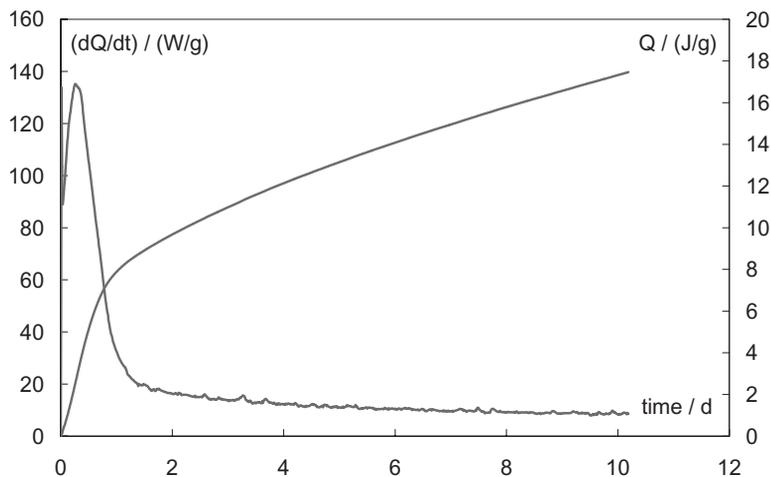


**Figure 1.15** Setup of a Thermal Activity Monitor, TAM (Thermometric/TA Instruments, Sweden/USA); right: one of up to four calorimeters insertable into the thermostat

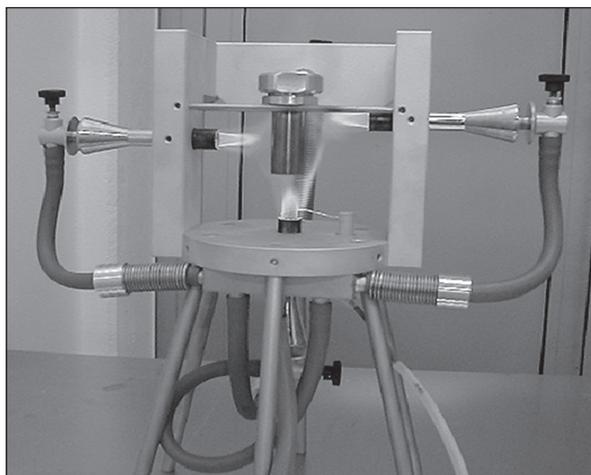
of a TAM system allows the detecting of very weak thermal effects even in the  $\mu\text{W}$  and  $\text{nW}$  range. This high sensitivity is achieved by a high precision temperature bath and a series of thermocouples controlling the temperature of sample and reference with an accuracy of at least  $10^{-4}$  K. Therefore, TAM systems are ideally suited for the investigation of long-term stabilities and compatibilities of energetic materials.<sup>64,73–74</sup> Figure 1.15 shows the setup of a typical TAM system. Up to four independently working calorimeters can be inserted into one high-precision thermostat. Each of them contains a sample of up to 3 g filled in special glass or steel ampoules.

As an example, Figure 1.16 shows the TAM measurement of the azido polymer GAP triol (the corresponding three-functional analog to GAP diol). The absolute heat and the heat flow rate were recorded for a period of 10 days at  $89^\circ\text{C}$ . The data show a typical equilibration process at the beginning of the measurement as it is often observed in TAM experiments. After inserting the calorimeter in the thermostat a certain time for thermal equilibration is required due to differences in heat capacity but also due to moisture or other impurities in the sample, and for other reasons. After equilibration only a low heat flow rate of  $10\text{--}20$  W/g is measured. Likewise, only a weak heat of  $18\text{J/g}$  was recorded after 10 days' storage at  $89^\circ\text{C}$ . Therefore, the GAP triol sample exhibits a sufficiently high thermal stability for storage and further processing. In case of thermally unstable compounds heat flow rates may reach values of several hundred W/g.

Experimental data obtained from isothermal mass loss experiments, adiabatic and isothermal heat flow calorimetry can be used for kinetic modeling and the prediction of life and storage time of energetic materials under different environmental conditions. However, the models, that such predictions are based on, are often very complex and thus not a result of simple extrapolation procedures. For example, different chemical pathways and mechanisms of decomposition reactions as well as aspects of autocatalysis must be considered.<sup>75</sup>



**Figure 1.16** TAM measurement of GAP triol at 89°C



**Figure 1.17** Koenen test setup. Courtesy of Prof. Dr Thomas Klapötke, Ludwig-Maximilians University, Munich, Germany

#### 1.4.6 Koenen Test

Besides analyzing the thermal sensitivity of energy-rich compounds under conditions of slow heating and pyrolysis by employing thermoanalytical techniques as described in other chapters, additional test procedures are available to determine the sensitivity of larger sample quantities to intense heating while being under confinement. The so-called Koenen Test (Steel Sleeve Test) is also used to determine the shipping classification of energetic (and non-energetic) compounds and to evaluate the degree of venting required to avoid an explosion during processing operations.<sup>24,76</sup>

A typical Koenen test setup is shown in Figure 1.17. The sample is filled into a non-reusable cylindrical steel sleeve which is closed by a metal plate with a variable orifice



**Figure 1.18** Steel sleeves used in Koenen tests: before (left) and after the test (right). Courtesy of Prof. Dr Thomas Klapötke, Ludwig-Maximilians University, Munich, Germany

**Table 1.5** Exemplary Koenen test results<sup>24</sup>

Explosive	Limiting diameter of the orifice / mm	Time until ignition / s	Time of combustion / s
Nitroglycerine	24	13	0
Pentaerythritol tetranitrate (PETN)	6	7	0
TNT	5	52	29
Ammonium nitrate	1	43	29

through which the decomposition gases can escape. The closing plate is secured with a nut. The diameter of the orifice can be varied between 1 and 20 mm and in case of sensitive materials the sample holder is not closed. The dimension of the steel sleeve is 25 mm OD × 24 mm ID × 75 mm length. The sample is loaded up to a filling height of 60 mm (sample volume: 27 mL). For the test the charged sample holder is heated simultaneously by four atmospheric burners.

The test is completed upon rupture of the steel sleeve or after heating the tube for a minimum of 5 minutes with no reaction. The elapsed time till ignition and the duration of the combustion are measured. With the variable orifice the limiting diameter is determined at which at least one explosion within a series of three consecutive experiments occurs and the sleeve is ruptured into three or more fragments (Figure 1.18). In Table 1.5 exemplary Koenen test results of common explosives are listed.<sup>24</sup>

## References

- [1] S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.*, **2005**, *44*, 5188–240.
- [2] E.F.V. Scriven, K. Turnbull, *Chem. Rev.*, **1988**, *88*, 297–368.
- [3] E.F.V. Scriven (ed.), *Azides and Nitrenes: Reactivity and Utility*, **1984**, Academic Press, Orlando, FL, USA.
- [4] H.C. Kolb, M.G. Finn, K.B. Sharpless, *Angew. Chem. Int. Ed.*, **2001**, *40*, 2004–21.
- [5] W.H. Binder, C. Kluger, *Curr. Org. Chem.*, **2006**, *10*, 1791–815.
- [6] I.J. Dagley, R.J. Spear, in: *Organic Energetic Compounds* (ed.: P.L. Marinkas), **1996**, Nova Science Publishers Inc., New York, USA.
- [7] R. Haiges, A. Boatz, A. Vij, M. Gerken, S. Schneider, T. Schroer, K.O. Christie, *Angew. Chem. Int. Ed.*, **2003**, *42*, 5847–51.
- [8] J.P. Agrawal, R.D. Hodgson, *Organic Chemistry of Explosives*, **2007**, John Wiley & Sons, Inc., New York, USA.
- [9] M.H.V. Huynh, M.A. Hiskey, D.E. Chavez, D.L. Naud, R.D. Gilardi, *J. Am. Chem. Soc.*, **2005**, *127*, 12537–43.
- [10] R. Escales, A. Stettbacher, *Initialexplosivstoffe*, **1917**, Verlag von Veit & Comp., Leipzig, Germany; p. 167.
- [11] M.E.C. Biffin, J. Miller, D.B. Paul, in: *The Chemistry of the Azido Group* (ed.: S. Patai), **1971**, Interscience Publishers, New York, USA.
- [12] F. Martin, *Über Azide und Fulminate*, **1913**, Darmstadt, Germany; cited in: T. Urbański, *Chemistry and Technology of Explosives*, **1964**, Pergamon Press, Oxford, Great Britain, Vol. III; p. 164.
- [13] M.B. Talawar, A.P. Agrawal, M. Anniyappan, D.S. Wani, M.K. Bansode, G.M. Gore, *J. Hazard. Mater.*, **2006**, *137*, 1074–8.
- [14] P.A.S. Smith, *The Chemistry of Open-Chain Organic Nitrogen Compounds*, Vol. 2, **1966**, W.A. Benjamin Inc., New York, USA, pp. 211–56.
- [15] G. Abbenante, G.T. Le, D.P. Fairlie, *Chem. Commun.*, **2007**, 4501–3.
- [16] G.R. Harvey, K.W. Ratts; Synthesis of azirenes from allenic esters; *J. Org. Chem.*, **1966**, *31*, 3907–10.
- [17] J.H. Boyer, F.C. Canter, *Chem. Rev.*, **1954**, *54*, 1–57.
- [18] E.E. Gilbert, *1,2,4,5-tetrakis (Diazidomethyl) benzene energetic polyazide*, United States Patent H000428.
- [19] T.M. Klapötke, B. Krumm, N. Mayr, F.X. Steemann, G. Steinhauser, *Safety Testing of Protective Gloves*, Proceedings of 11<sup>th</sup> International Seminar on New Trends in Research of Energetic Materials, **2008**, Pardubice, Czech Republic, pp. 597–605.
- [20] J.S. Rinehart, J. Pearson, *Explosive Working of Metals*, **1963**, Pergamon Press, Oxford, Great Britain; p. 38.
- [21] NATO STANAG 4489 Document Information, Explosives, Impact Sensitivity Tests, **1999**.
- [22] Department of Defence Test Method Standard, *Safety and Performance Tests for the Qualification of Explosives (High Explosives, Propellants and Pyrotechnics)*, MIL-STD-1751A, **2001**; Superseding MIL-STD-1751(USAF), **1982**.
- [23] P.W. Cooper, S.R. Kurowski, *Introduction to the Technology of Explosives*, **1996**, John Wiley & Sons, Inc., New York, USA.
- [24] R. Meyer, J. Köhler, A. Homburg, *Explosives*, **2007**, 6<sup>th</sup> revised edition, Wiley-VCH, Weinheim, Germany.
- [25] C.-O. Leiber, B. Dobratz, *Assessment of Safety and Risk with a Microscopic Model of Detonation*, **2003**, Elsevier, Amsterdam, The Netherlands.
- [26] F.P. Bowden, A. Yoffe, Hot spots and the initiation of explosion, *Proceed. Symposium on Combustion and Flame, and Explosion Phenomena*, Vol. 3, **1949**, Cambridge, MA, USA.
- [27] T.M. Klapötke, C.M. Rienäcker, *Propellants Explosives and Pyrotechnics*, **2001**, *26*, 43–7.
- [28] M.J. Kamlet, H.G. Adolph, *Propellants Explosives and Pyrotechnics*, **1979**, *4*, 30–4.
- [29] J. Mullay, *Propellants Explosives and Pyrotechnics*, **1987**, *12*, 60–3.

- [30] M.H.V. Huynh, M.A. Hiskey, T.J. Meyer, M. Wetzler, *Proc. Natl. Acad. Sci. USA*, **2006**, *103*, 5409–12.
- [31] M.H. Keshavarz, *J. Hazard. Mater.*, **2007**, *148*, 648–52.
- [32] M.H. Keshavarz, H.R. Pouretedal, A. Semnani, *J. Hazard. Mater.*, **2007**, *141*, 803–7.
- [33] M.H. Keshavarz, H.R. Pouretedal, *J. Hazard. Mater.*, **2005**, *124*, 27–33.
- [34] L. Türker, *J. Mol. Struct.: THEOCHEM*, **2005**, *725*, 85–7.
- [35] S. Ye, K. Tonokura, M. Koshi, *Combust. Flame*, **2003**, *132*, 240–6.
- [36] G. Su-Hong, C. Xin-Lu, W. Li-Sha, Y. Xiang-Dong, *J. Mol. Struct.: THEOCHEM*, **2007**, *809*, 55–60.
- [37] R. Sundararajan, S.R. Jain, *Indian J. Technol.*, **1983**, *21*, 474–7.
- [38] M. Vaullerin, A. Espagnacq, L. Morin-Allory, *Propellants Explosives and Pyrotechnics*, **1998**, *23*, 237–9.
- [39] M. Cartwright, J. Wilkinson, *Correlation of Structure and Sensitivity in Azides*, **2008**, Cranfield CERES Publication (<https://dspace.lib.cranfield.ac.uk/handle/1826/2584>).
- [40] H. Koenen, K. H. Ide, *Explosivstoffe*, Bd. 9, **1961**, Erwin Barth Verlag KG, Mannheim, Germany, pp. 4–13 and 30–42.
- [41] NATO STANAG 4487 Document Information, *Explosives, Friction Sensitivity Tests*, **2002**.
- [42] NATO STANAG 4490 Document Information, *Explosives, Electrostatic Discharge Sensitivity Tests*, **2001**.
- [43] NATO STANAG 4239 Document Information, *Electrostatic Discharge, Munitions Test Procedures*, **1997**.
- [44] NATO AOP-24 Document Information, *Electrostatic Discharge, Munition Assessment and Test Procedures*, **1998**.
- [45] S. Amari, F. Hosoya, Y. Mizushima, T. Yoshida, *Electrostatic Spark Ignitability of Energetic Materials*, **1995**, 21st International Pyrotechnic Seminar, Moscow, Russia, 13–31.
- [46] B.T. Fedoroff, O.E. Sheffield, *Encyclopedia of Explosives and Related Items PATR 2700*, Vol. 5, **1972**, Picatinny Arsenal, Dover, N.J., USA.
- [47] D. Skinner, D. Olson, A. Block-Bolten, *Propellants Explosives and Pyrotechnics*, **1998**, *23*, 34–42.
- [48] M. Roux, M. Auzanneau, C. Brassy, *Propellants Explosives and Pyrotechnics*, **1993**, *18*, 317–24.
- [49] M. Auzanneau, M. Roux, *Propellants Explosives and Pyrotechnics*, **1995**, *20*, 96–101.
- [50] C.J. Dahn, B.N. Reyes, A. Kashani, J. Finkelstein, Electrostatic hazards of explosive, propellant and pyrotechnic powders, **1998**, *Proceed. 20<sup>th</sup> Electrical Overstress/ Electrostatic Discharge Symposium*, Reno, Nevada, USA; 139–50.
- [51] M.E. Brown, *Introduction to Thermal Analysis: Techniques and Applications*, **2001**, Kluwer Academic Publishers, Norwell, MA, USA.
- [52] B. Wunderlich, *Thermal Analysis*, **1990**, Academic Press, San Diego, CA, USA.
- [53] W.W. Wendlandt, *Thermal Analysis*, **1986**, John Wiley & Sons, Inc., New York, NY, USA.
- [54] G.W.H. Höhne, W.F. Hemminger, H.-J. Flammersheim, *Differential Scanning Calorimetry*, **2003**, Springer, Heidelberg, Germany.
- [55] S. Löbbecke, M. Kaiser, G.A. Chiganova, in: *Energetic Materials: Particle Processing and Characterization* (ed.: U. Teipel), **2004**, Wiley, Weinheim, Germany.
- [56] D.R. Miller, D.C. Swenson, E.G. Gillan, *J. Am. Chem. Soc.*, **2004**, *126*, 5372–3.
- [57] T. Keicher, G. Unkelbach, H. Krause, Synthesis and characterization of new triazido-plasticizers, **2005**, *Proceed. 36<sup>th</sup> Int. Annual Conference ICT*, Karlsruhe, Germany; pp. 49/1–8.
- [58] D. Rösling, G. Unkelbach, T. Keicher, H. Krause, Synthesis, characterization and first formulations of new triazidoplasticizers, **2007**, *Proceed. NTREM Conference – New Trends in Research of Energetic Materials*, Pardubice, Czech Republic, 943–50.
- [59] A. Pfeil, S. Löbbecke, *Propellants Explosives and Pyrotechnics*, **1997**, *22*, 137–42.
- [60] C.I. Schilling, S. Bräse, *Org. Biomol. Chem.*, **2007**, *5*, 3586–8.
- [61] S. Löbbecke, H. Schuppler, W. Schweikert, *J. Therm. Anal. Calorim.*, **2003**, *72*, 453–63.
- [62] B. Vogelsanger, *Chimia*, **2004**, *58*, 401–8.
- [63] F. Stoessel, *Thermal Safety of Chemical Processes*, **2008**, Wiley-VCH, Germany.

- [64] M.W. Whitmore, J.K. Wilberforce, *J. Loss Prev. Process Ind.*, **1993**, 6, 95–101.
- [65] Bundesamt für Wehrtechnik und Beschaffung, *Arbeitsvorschriften für die chemische und physikalische Untersuchung von Treibladungspulver (TLP) 2.31.1 Bestimmung der chemischen Beständigkeit bei 90°C und 75°C*, **1999**, Technische Lieferungsbedingung TL 1376-0600/430.
- [66] M.A. Bohn, Decomposition behaviour of azido based and nitric acid ester based plasticizers and binders determined by adiabatic selfheating, **1998**, *Proceed. 11<sup>th</sup> Symposium on Chemical Problems Connected with the Stability of Explosives*, Båstad, Sweden; 61–88.
- [67] D.I. Townsend, *Accelerating Rate Calorimetry*, **1981**, I.Chem.E. Symposium Series 68.
- [68] D.I. Townsend, J.C. Tou, *Thermochim. Acta*, **1980**, 37, 1–30.
- [69] X.-R. Li, H. Koseki, *J. Loss Prev. Process Ind.*, **2005**, 18, 455–9.
- [70] M.A. Bohn, Heat generation of propellants & explosives, **1994**, *Proceed. Int. Symp. on Energetic Materials Technology*, Orlando, USA.
- [71] J. Suurkuusk, I. Wadsö, *Chemica Scripta*, **1982**, 20, 155–63.
- [72] P. Bäckman, M. Bastos, L.E. Briggner, *et al.*, *Pure Appl. Chem.*, **1994**, 66, 375–82.
- [73] NATO STANAG 4582 Document Information, *Explosives, single, double and triple base propellants*, **2004**.
- [74] NATO STANAG 4147 Document Information, *Chemical compatibility of ammunition components with explosives and propellants*, **2001**.
- [75] M.A. Bohn, Modelling of the stability, ageing and thermal decomposition of energetic components and formulations using mass loss and heat generation, **2000**, *Proceed. 27<sup>th</sup> Int. Pyrotechnics Seminar*, Grand Junction, Colorado, USA; 751–70.
- [76] United Nations, *Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria*, **2003**, 4th revised edition, New York and Geneva.